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BLOOD GROUPS

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INTRODUCTION

Scientific progress in biological sciences, including medicine, is based on the application of two principles, which at first glance may appear contradictory, but which actually complement each other:

1.) More and finer differences are being found in certain areas of scientific investigation, and then or concomitantly, more and more similarities are being discovered.

2.) In order to study an object thoroughly, one has to find differences, with ever increasing details. Finding of similarities is the way to arrive at generalizations.

One can trace these two principles in practically every phase of the development of medicine. For example, differances in various characteristics of the pulse were no doubt observed by the earliest physicians. Then it was noted that some of these features were found in certain individuals. In this way certain categories of observations of the pulse were collected and correlated with certain disease manifestations. The same principle can be applied throughout medical history, up to and including the most modern developments.

The primitive mind strove to increase knowledge and gather information. This was done in a crude fashion, but the principle of difference and similarities applied even to that early period. It may be that the beliefs in "pure and impure" blood date from these early ages of man's history. It would be logical to trace taboos to such beginnings; some of these have been revived from time to time in history, even after the onset of scientific medicine. The Spanish conception of blood purity, *limpezza*, preceding and during the bloody inquisition, the Nazi ideas about blood purity, are all throwbacks to the archaic period of groping after differences and similarities.

With the advent of more scientific methods of study, the finding of differences assumed a more precise and objective character. As would be expected, with the discovery of the microscope, morphologic differences were found. Then followed an era of chemical differentiation, finding more and more chemical differences and similarities.

When blood chemistry studies were begun, they, too, marked progress by the finding of differences and similarities. The same applied to the development of clinical bacteriology and blood morphology. The finding of certain blood cells common to most people, and of other exceptional types, and then the grouping of the latter together, marked progress.

The most recent discovery, serologic differentiation, is based on observations in which antigen-antibody reactions are involved. Here the principle of differences and similarities is particularly well illustrated: in the development of our knowledge of blood groups, both features

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Table 1.

Distribution of Blood Groups

Red Blood Cells					Serum	
Classification					Isoagglutinins	
Jansky	Moss	International	Incidence	Sub-groups	Natural	Irregular
IV	I	AB	5%	A_1B	O	α_2-(Anti-O) (Anti-A_2)
		(Universal Recipient)		A_2B	O	α_1-(Anti-A_1)
II	II	A	40%	A_1	Anti-B	α_2-(Anti-O) (Anti-A_2)
				A_2	Anti-B	α_1-(Anti-A_1)
III	III	B	10%	-	Anti-A	
I	IV	O (Universal Donor)	40%	-	Anti-A Anti-B	

If A_2 is not recognized - it is taken for O (false Universal Donor)
If A_2B is not recognized - it is taken for B.

are exemplified, *i.e.*, the differences between individuals and the similarities which permit us to assemble them in groups.

Interest in blood differences and similarities goes back to the most ancient periods of human history. We refer briefly to the years following Harvey's discovery of circulation of blood in 1616, and the publication of his results in 1628. Soon after this discovery, records of attempted blood transfusions began accumulating. Of these, the first attempts were performed on animals, especially dogs. The first properly recorded transfusion in man dates back to 1667, and was performed by the French physician, Jean-Baptiste Denis. He injected nine ounces of blood from the carotid artery of a lamb into the vein of a young man, and remarkably, this transfusion was successful. He did report that in some of his transfusions, patients passed urine, "black as soot." We now know that this indicated that the recipients had hemolytic transfusion reactions.

It is interesting to record details of one of his transfusion experiences. Denis gave his fourth patient two transfusions. The indication was a mental disturbance, which he claimed improved after the transfusion. The first transfusion was uneventful, but following the second transfusion, "his arm became hot, the pulse rose, sweat burst out over his forehead, he complained of pain in the kidneys, and was sick in the stomach. The next day the urine was very dark, in fact black." This report sounds like a perfect description of what we now know as a hemolytic transfusion reaction. Denis continues that he then gave a third transfusion to the same patient at the request of the patient's wife, and the patient died.

It was unavoidable that these and similar attempts led to serious conse-

quences for the patient, and eventually transfusions were prohibited in France, except with the sanction of the Faculty of Medicine in Paris. Later an edict of the French parliament prohibited transfusions. As a result of these events, a standstill in the use of transfusions apparently followed for about 150 years. During that time, very little was written about the subject.

It was not until the 19th century that a new era in the administration of blood began. In October, 1818, James Blundell, an English obstetrician at Guy's Hospital, gave the first transfusion from man to man.

During the last quarter of the 19th century, observations began accumulating, indicating differences in the blood of human beings. Observers described that clumping occurred when the blood of two persons was mixed. This was attributed to disease. First one, then more and more diseases were claimed to be identifiable by blood clumping. This eventually led to the absurd conclusion that this phenomenon was applicable to most diseases. This was the situation, when Landsteiner reported in 1900, that the phenomenon of clumping is not due to disease but is rather a physiologic manifestation due to the presence of agglutinable substances in red blood cells and to agglutinins in the plasma[1]. His more extensive article on the subject was published in 1901. By this discovery, Landsteiner laid the foundation for a new science, which found application far beyond the field of blood transfusions.

BLOOD FACTORS A AND B

Landsteiner and his associates discovered the existence of two specific substances, blood group factors, in red cells of man; by their presence, whether singly or together, or by their absence, they form the four so-called Landsteiner or international blood groups[1]. *Table* 1 presents the distribution of these blood group factors. The persons who have blood group factor A belong to blood group A, those who have factor B belong to blood group B, those who have both factors belong to blood group AB, and those who have neither belong to blood group 0. (We became used to reading the latter designation as O, whereas actually it means zero.) The distribution of these blood group factors varies in different races. The incidence, as given in *Table* 1, applies to the Caucasoid population of this country. Racial differences are shown in *Table* 2. The blood group factors are inherited characteristics; A and B are transmitted as Mendelian dominants. O, the absence of the blood factors, is a recessive characteristic.

Table 2

RACIAL DISTRIBUTION OF BLOOD GROUPS

Types	O	A	B
I. European	39	43	12
II. Intermediate (Arabs, Turks, Russians, etc.	40	33	20
III. Human (Japan, South China, Hungary, Roumanian Jews)	28	39	19
IV. Hindo-Manchu (Korea, North China, Gypsies, Hindus)	30	19	39
V. Afro-South Asiatic (Negroes, Madagascans, Malayans)	42	24	28
VI. Pacifico-American (Indians, Australians, Filipinos, Icelanders)	67	29	3

The recognition of a blood group factor of the ABO system is done with the help of agglutinins of the blood plasma capable of reacting with the blood factors. These are anti-A and anti-B. Their presence in the blood plasma is recorded in *Table* 1. Every person has the agglutinin for the blood factor which he does not possess in his blood. The term isoagglutinin designates that antibody and antigen are in the same species.

There are occasional individuals with defective blood group formulas, *i.e.*, a person of blood group A who lacks anti-B, or a person of blood group O who has only anti-A or anti-B. Such defects are rare.

Whereas blood group properties are, almost without exception, present at birth, the isoagglutinins are absent at birth and develop as part of the growth process. They usually appear from six months to a year. This gradual development has been described by Hirszfeld[2] as serologic maturation. Just as we undergo physical and mental maturation, so we undergo a process of serologic maturation. What it is that makes antibodies appear at a certain time of our growth is not fully known.

Blood group properties A and B are

present not only in the red blood cells, but also in most other tissues of man. This will be discussed later. They are also present in animals and are distributed all over organic nature in a fashion which is not clearly understood; they are also present in large quantities in peptone. It is possible that the development of the isoagglutinins is the result of immunization to which the infant is exposed in the course of intake of food, etc. It is interesting that the isoagglutinins, which can be measured by means of titration, vary in strength in certain conditions in various individuals. On the whole, they seem to increase in titer and reach a peak approximately at puberty. They then remain at a fairly constant level until about the age of 50, when they gradually begin to decline.

The blood factors are antigens. They may produce an increase of antibodies when injected into human beings who lack the same antigens. They regularly produce antibodies when injected into certain animals. The strength of the antigenic properties of the blood factors can be measured by their ability to absorb their corresponding antibodies. Whereas the variations in the strength of the isoagglutinins follow the pattern just described above, it is more difficult to demonstrate a similar pattern with regard to the blood factors, as the antigen concentration of blood factors varies in different individuals. On the whole, the antigenic properties of the blood factors are less developed at birth. This is especially applicable to blood factor A, which occurs in several forms differing in reactivity.

Subgroups of A. Whereas factor B is a single entity, factor A consists of several variants. Two of these, A_1 and A_2, are particularly well known. A_1 is present in about eighty per cent of persons belonging to group A, and in about sixty-seven per cent of those belonging to group AB. These are known as subgroups A_1 and A_1B, respectively. The remainder belong to subgroups A_2 and A_2B. Red cells of groups A_2 and A_2B react slowly and weakly with serums containing the corresponding isoagglutinin. These corresponding isoagglutinins are anti-A_1, which reacts specifically with red cells of subgroups A_1 and A_1B; and anti-A_2, which reacts specifically with subgroups A_2 and A_2B. It was found that the serum containing anti-A_2 reacts not only with cells of subgroup A_2, but also with cells of group O. This observation led to the recognition of a special blood group substance in group O, and not merely the absence of A and B as had been assumed earlier. The differences between A_1 and A_2 and between A_1B and A_2B are qualitative and not just quantitative, because anti-A_2 may be present in the blood of groups A_1 and A_1B and conversely, anti-A_1 may be present in groups A_2 and A_2B. In the course of time it was also found that there are more subgroups in addition to A_1 and A_2. These additional subgroups, A_3, A_4, etc., are extremely rare and difficult to detect.

In general, the antigenic properties in subgroup A_1 are stronger when the A is present by itself than when it is present with B in subgroups A_1B, A_2B, etc. In other words, factor A_2 reacts more weakly when it is combined with B in subgroup A_2B than when alone in subgroup A_2. These observations have an important bearing on possible errors which are due to failure in detecting the weaker reacting subgroups. Such errors may lead to the reporting of O, when actually one is dealing with A_2 or A_3, or of B, when A_2B or A_3B is present. In recent years, due to the standardization of testing serums by the National Institutes of Health, this menace is less serious than previously, when every laboratory produced its own testing serums. Compliance with regulations of the National Institutes of Health has added immeasurably to the safety of blood transfusions.

Isoagglutinins anti-A and anti-B react strongest at lower temperatures, quite distinctly, though less strongly, at room temperature, and considerably less at body temperature. The irregular isoagglutinins mentioned previously as anti-A_1 and anti-A_2 react much stronger at icebox temperature and rarely, if at all, at room temperature. They belong to the group of so-called "cold agglutinins." This is the reason why one does

not need to consider subgroups in selection of donors for blood transfusions.

In the course of time, much has been learned about the blood group factors. They are present at birth and have actually been found in fetuses a few months old. They continue unchanged throughout life and are not influenced by endogenous or exogenous changes. No injections, drugs or diseases can alter them. As long as the body is not decomposed, they continue to be detectable after death. It was possible to detect them in Egyptian and Indian mummies several thousand years old.

The blood group factors are present not only in the red blood cells, but in practically all tissues. They are found in two forms, as alcohol soluble blood group substances, which are present in all persons, and as water soluble substances, which are present in only some persons (in about eighty per cent). The latter, known as secretors, have the ability to secrete the blood group substances in saliva, gastric juice, etc. In this way, people are divided into two groups, secretors and non-secretors. The property of secreting is an inherited Mendelian dominant characteristic, as are the blood group factors in general. Its relation to a new blood group factor (Lewis) will be discussed later.

The quantities of blood group substances vary in different tissues. For example, the largest amounts, even more than in the blood, are present in the salivary glands and the pancreas; very little, if any, are detectable in the central nervous system tissues. The other tissues occupy intermediate positions.

Tests for blood group factors ABO. These tests are simple and depend on the mixing of small amounts of serum containing the isoagglutinins anti-A and anti-B, with similar amounts of suspensions of red blood cells. The tests are run at room temperature, on a slide, or preferably in a test tube. *Table* 3 shows how the results of these tests determine the presence of the blood group factors.

A complete blood grouping includes testing for the blood group factor in the red cells with potent serums containing isoagglutinins (blood grouping), and testing for isoagglutinins in the serum with known red cells of known blood group composition (check grouping). As controls, serum of group O, which contains anti-A and anti-B, is used, and in the second part of the test, red blood cells of group O, which are neither agglutinated by anti-A nor anti-B, are used. Such control tests offer the best safeguard against errors.

Application to blood transfusions. Selection of donors, for blood transfusion, is based on the principle that individuals of the same blood group as the recipient be selected, and that their blood be matched with recipient's blood in two tests. These are:

(1) The so-called "major crossmatch," in which the serum of the recipient is mixed with the red blood cells of the donor. Any clumping, no matter how feeble, eliminates the donor.

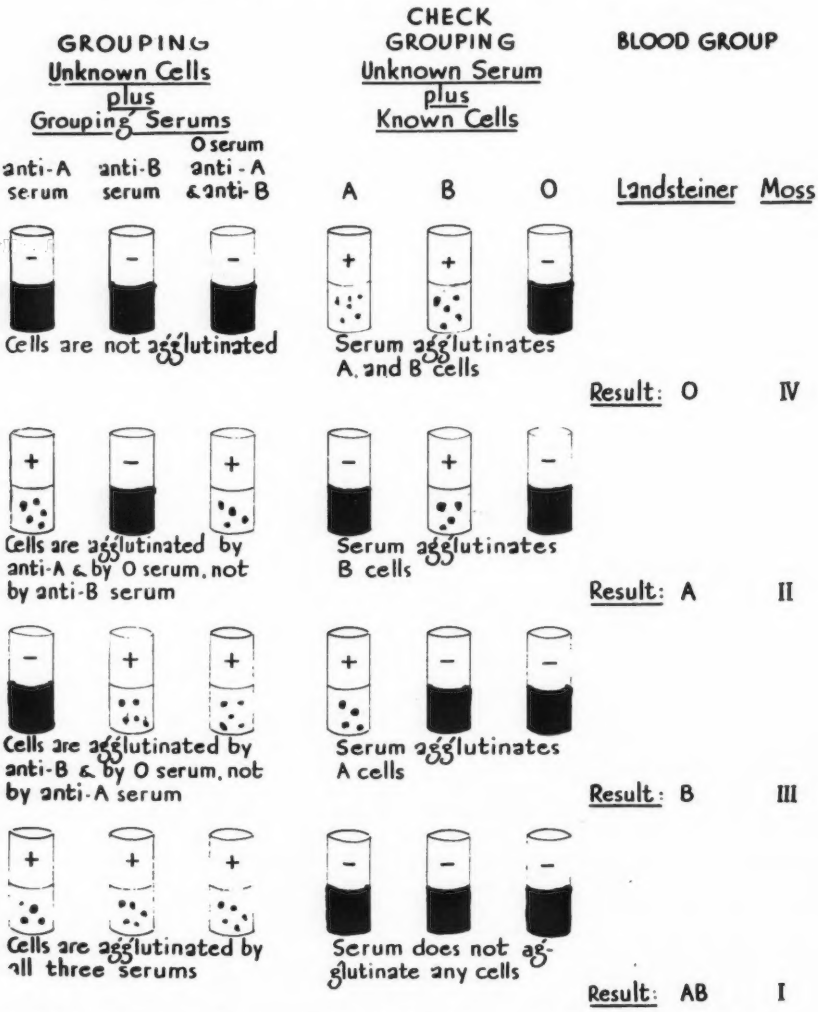
(2) The so-called "minor crossmatch," in which the serum of the donor is tested with the red blood cells of the recipient. Here, too, no clumping should be present, except in the case of the so-called "universal donor." The record of this procedure, together with the record of the blood groupings of the recipient and donor, is entered in the hospital record and becomes a permanent part of it.

The reason for the designation of these two tests as "major" and "minor" is that the first one establishes a possible reaction between the antibodies in the whole volume of the plasma of the recipient, with the relatively small volume of transfused red cells. In the case of a reaction, the danger is much greater than the reaction depicted in the second test, where the possibility of an agglutination between the rapidly diluted, small amount of the donor's plasma with the larger amount of the recipient's red blood cells is considered. Theoretically, it is assumed that the second reaction would be less dangerous, due to the effect of dilution on the injected antibody. It is this reasoning which gave rise to the conception of the so-called "universal donor" of group O. In this group, under usual circumstances, no agglutinable substances are present in the red cells. Thus, it was assumed that the isoagglu-

tinins, anti-A and anti-B, present in the donors' plasma, would become rapidly diluted in the plasma of the recipient, thereby eliminating any serious consequences. This reasoning still applies in most instances, but there are occasional individuals of group O whose isoagglutinin titer is exceptionally high. In these

TABLE 3

BLOOD GROUPING TESTS



NOTE: Results of grouping and check grouping must be identical. Otherwise test is invalid.

Exception: In infants agglutinins in serum may be absent.

cases, the dilution resulting from the transfusion of one pint of blood to a person with about ten to twelve pints of blood, is not sufficient to eliminate the possibility of a reaction, resulting from the combination of these antibodies with the recipient's red cells. Actually, transfusion reactions, even fatal ones, have been observed under these circumstances. Therefore, the use of the so-called "universal donor" has been restricted to donors with low titers of isoagglutinins.

It has been recommended that the titer of these antibodies in the plasma of group O donors, for recipients of different blood groups, be determined by means of a rough titration which shows if the antibodies against A or B are present in a titer, set arbitrarily at 1:100 to 1:200. An individual with a titer below this level is considered as meeting the requirements of a so-called "universal donor." However, more recently, it was found that in addition to natural isagglutinins, some individuals have so-called "immune" isoagglutinins. These immune isoagglutinins are much more dangerous than natural ones, even if present in very low titers. Some fatal transfusion reactions have actually been traced to the presence of these. The main reasons why "immune" isoagglutinins are more dangerous than the natural ones, are their enhanced reactivity at body temperature and their resistance to neutralization.

Witebsky[3] described a method of detecting these immune isoagglutinins, by adding to such a serum a certain amount of soluble blood group specific substances. They neutralize the natural isoagglutinins only; they do not neutralize the isoagglutinins of immune origin, or do it much less efficiently. These immune isoagglutinins can be detected by using diluents other than saline. A test was recently described by Grove-Rasmussen[4] which makes it possible to detect immune antibodies in a simple cross-matching test. If any agglutination in this test is present, the donor is unacceptable. Further restriction in the use of the "universal donor" due to consideration of the Rh factor will be mentioned later.

The selection of suitable donors is not limited to the principle of blood group compatibility. Other tests are done in order to eliminate the possibility of the transmission of certain diseases, including syphilis, malaria, and especially, homologous serum jaundice. The donor also has to meet certain physical requirements in order to protect him against complications resulting from the removal of an amount of blood that might be excessive for his physical condition. These tests include a thorough medical history, physical examination, tests for hemoglobin, etc. For the protection of recipients and donors, standards have been set up by the National Institutes of Health and by the American Association of Blood Banks.

BLOOD FACTORS M AND N

In 1927, Landsteiner and Levine[5] discovered two more blood factors, M and N. These factors are present either singly (the former in about thirty per cent of the Caucasoid population, the latter in twenty per cent) or together (in the remaining fifty per cent). Whereas a large proportion of the population lacks A and B factors (about forty-five per cent), no one lacks the M or N factor. The M and N factors have found no application in clinical medicine, because only rarely are there natural agglutinins against them[6], and none are produced when blood M is injected into recipients N, and vice versa. In other words, the M and N factors are not antigenic in man. They have found application in legal medicine; this will be discussed later.

THE Rh FACTOR

A great advance was made in 1940, when Karl Landsteiner and Alexander Wiener[7] discovered a new blood factor, known as Rh, by injecting the blood of the Rhesus monkey (*Macaca rhesus*) into rabbits. The antibodies so produced in rabbits, reacted with about eighty-five per cent of random human blood samples. The designation of the new blood factor, Rh, was taken from the first two letters of the name of the monkey. The eighty-five per cent of Caucasoids with the Rh factor, are called Rh-positive, and the fifteen per cent who lack it, Rh-negative. This discovery became important because it not only contributed greatly

to the safety of blood transfusions, but because it helped us to understand, recognize and treat fetal erythroblastosis, or hemolytic disease of the newborn.

Properties of the Rh factor. The Rh factor shows racial differences similar to the ABO factors. For example, the incidence of Rh-negativity is lower in Negroes than Caucasoids, and still lower in Mongoloids. Only about one per cent of Chinese are Rh-negative.

Normally, there are no isoagglutinins against the Rh factor. Therefore, theoretically one should be able to inject Rh-positive blood into Rh-negative recipients with impunity, just as one does with M and N blood. However, it was found that whereas M and N are not antigenic in man, the Rh factor is antigenic, and Rh-negative persons injected with Rh-positive blood develop antibodies. This process of developing antibodies is called sensitization.

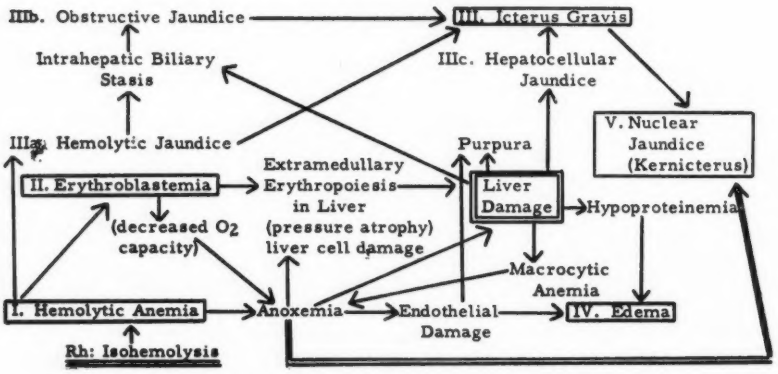
The Rh factor is present at birth in practically the same strength as in adulthood and continues to be present all throughout life.

The Rh factor is apparently limited to red cells; although its presence in other tissues has been claimed, the methods of detecting it are unsatisfactory. It is definitely present in amniotic fluid.

Application of the Rh factor to blood transfusions. The selection of donors according to their ABO blood factors, as described previously, has made blood transfusions relatively safe. However, it was known that in spite of all precautions in selecting donors, occasionally reactions occurred which could not be accounted for even if donor and recipient belonged to the identical group. This was particularly noted in individuals who had received more than one transfusion. Occasionally it was seen in recipients receiving their first transfusion, but only in women who were pregnant at the time of the transfusion, or who had been pregnant in the more or less distant past. No explanation was forthcoming for these unexpected and sometimes fatal transfusion reactions. Wiener was the first one to observe that individuals manifesting such unexplained transfusion reactions had antibodies, which behaved just like the antibodies produced in rabbits immunized with blood of the Rhesus monkey[8]. Before the discovery of the Rh factor by Landsteiner and Wiener, Levine furnished the explanation for

TABLE 4

PATHOGENESIS OF FETAL ERYTHROBLASTOSIS



Pathogenesis of fetal erythroblastosis. Principle: An Rh-positive husband of an Rh-negative woman transmits the Rh factor to the fetus. Rh-antigenic substances pass from an Rh-positive fetus through the placenta and produce the Rh antibodies in the mother. The latter pass from the mother to the fetus through the placenta, act in the fetus as hemolytic agents and start the sequence of interlocking pathologic changes as presented in this chart.

transfusion reactions in women receiving even the first transfusion[9]. He reported a case of a woman who aborted, and who was later given a transfusion of her husband's blood. Following the transfusion she developed an almost fatal hemolytic reaction. Levine found antibodies in her blood, which reacted similarly to Rh antibodies, with blood specimens collected at random. This led to the recognition that Rh-negative women, pregnant with an Rh-positive fetus, may become sensitized by transplacental passage of Rh factor elements. Such women may develop Rh antibodies, and when given Rh-positive blood may develop hemolytic transfusion reactions of varying degrees of severity. These discoveries have cleared up the mystery of most unexpected transfusion reactions and showed the way to prevent them.

The reason why the incompatibility responsible for these two types of transfusion reactions was not detected earlier, was that the usual method of doing cross-matching tests, at room temperature, and with saline as diluent for the serum and as a suspension medium for the red cells, is frequently not suitable for the detection of Rh antibodies.

Application to fetal erythroblastosis. The pathogenesis of fetal erythroblastosis has been discussed in a previous article published in *The Chicago Medical School Quarterly*[10]. There is no need to repeat the data already published, but briefly summarized, Rh factor studies have resulted in clarification of the pathogenesis of fetal erythroblastosis, as represented in *Table* 4.

As a rule, the diagnosis of fetal erythroblastosis presents no difficulty, but

Table 5

Differential Diagnosis of Fetal Erythroblastosis in Live Born Infants

	F.E.[1]	C.S.	A.I.	P.I.	I.D.	I.N.	I.P.	PJK***	H.D.N.	C.M.B.D.	C.M.H.
1. Familial incidence	+++	+	-	-	-	±	+		-	-	-
2. Splenomegaly	+++	+++	+	±	+	+	±	-	-	-	+
3. Hepatomegaly	++	++	±	±	+	-	±	-	-	+	+
4. Enlarged placenta*	±	++	-	-	-	-	-	-	-	-	-
5. Anemia	++	++	++	±	+	-	±	-	±	-	-
6. Leukocytosis	++	++	++	++	+	-	±	-	±	-	-
7. Leukemoid blood picture	++	++	++	+	+	-	-	-	±	-	-
8. Erythroblastemia**	++	++	+	-	+	-	-	±	±	-	+
9. Severe and early jaundice	++	++	+	+	+	-	-	- (+3rd day or later)	-	-	-
10. High blood bilirubin	++	++	+	+	+	+	+		-	+	-
11. Indirect van den Bergh reaction	++	++	+	±	+	+	+		-	-	-
12. Bile in urine	++	++	+	-	+	-	±		-	+++	-
13. Purpura	±	+	±	±	±	-	-	+(lung, brain)	+++	+	-
14. Edema, general	±	+	-	-	-	-	-	-	-	-	-
15. Edema, local	±	+	-	-	±	-	-		-	-	-
16. Extramedullary hematopoiesis at term	+++	+++	±	-	+	-	-	-	-	-	+
17. Hepatic biliary stasis	+++	+++	+	-	+	-	+	-	-	+++	-
18. Liver cell damage	+++	+++	±	±	+	-	-	-	-	+++	-
19. Hemosiderosis	+++	+++	±	±	+	-	-	-	-	-	-
20. Nuclear jaundice (Kernicterus)	+	-	-	-	-	-	-	+	-	-	-
21. Positive tests for syphilis	-	+++	-	-	-	-	-	-	-	-	-
22. Father Rh+, mother Rh-, infant Rh+	++ (in 95%)	-	-	-	-	-	-	-	-	-	-
23. Rh antibodies in mother's blood	++ (in over 90%)	-	-	-	-	-	-	-	-	-	-
24. Coombs test	+	-	-	-	-	-	-		-	-	-

+++always present; ++rarely absent; +frequently present; ±may be present; -absent.

[1]Abbreviations: F.E. -Fetal erythroblastosis; C.S. -Congenital syphilis; A.I. -Antenatal infection; P.I. -Postnatal infection; I.D. -Inclusion disease; I.N. -Icterus neonatorum; I.P. -Icterus praecox; PJK-PJK syndrome or sixth day disease; H.D.N. -Hemorrhagic disease of newborn; C.M.B.D. -Congenital malformation of bile ducts; C.M.H. -Congenital malformation of heart.

*The average weight of a normal placenta is about one-seventh of the total body weight.

**Erythroblastemia indicates the presence of immature nucleated erythrocytes in the circulation in excess of 1000 per cu. mm.

***Prematurity-Jaundice-Kernicterus syndrome; new entity in premature babies (Aidin, Read: Med. Press, 226: 88-93, 1951).

there are cases in which the diagnosis is not easy. This refers particularly to so-called "occult" or latent fetal erythroblastosis, in which early diagnosis is particularly important because proper therapy may be lifesaving. The various differential diagnostic problems are shown in *Table* 5. In the case of latent fetal erythroblastosis, in which the newborn baby presents no clinical signs of disease, the examination of cord blood permits the diagnosis if the red cell count is four and one-half million or less, the hemoglobin fourteen grams or less, and the Rh factor and the Coombs test are positive. The positive direct Coombs test is no doubt, the most important of these, because it establishes that the red blood cells are coated with antibodies. In such cases, energetic therapy is indicated. The quantitative bilirubin in the serum is important prognostically.

The treatment of hemolytic disease of the newborn has undergone radical changes in recent years. The emphasis is now on exchange transfusion, with one or more units of blood being exchanged, the amount depending on the severity of the jaundice. If the serum bilirubin is between sixteen and twenty mg% or more, one unit is not sufficient. Furthermore, if repetition of the test for serum bilirubin shows continued high levels or an elevation, and the Coombs test continues to be positive, another replacement transfusion is indicated as soon as possible, preferably within twelve hours after the first.

Rh-negative blood of an ABO group compatible with the blood of the mother is used. Blood compatible with the mother is chosen, because the newborn has no isoantibodies except those received from the mother. If the baby is of a group different than O, and O blood is used, blood group specific substances are added in order to neutralize the isoantibodies. Recent experience indicates that severe jaundice is prognostically much more serious than anemia. It has also been recognized that one must take care not to increase the blood volume of the infant excessively, because heart failure may supervene. In order to increase the volume of red cells, without increasing the blood volume, it has been found useful to remove a portion of the plasma from the blood after centrifugation or sedimentation. In this way the hematocrit of the transfused blood is raised to fifty-five or sixty. An exchange of equal volumes, with this high hematocrit blood, permits a greater replacement of the Coombs test positive red cells with O Rh-negative blood of the donor.

Because of the presence of Rh antibodies in the mother's milk, the present consensus is not to permit nursing of babies with hemolytic disease of the newborn. The opposite view, recently expressed by some authors, is that it is safe for mothers of babies with erythroblastosis to nurse the infants, because the mucous membrane of the upper gastro-intestinal tract is not permeable. However, until such time that this problem has been fully settled, it appears safer to recommend that the previously held view be followed.

For the time being, the only reliable means of preventing fetal erythroblastosis is to make sure that women or girls, regardless of age, are always given Rh compatible blood. The disease is rare in the first-born and in many cases previous sensitization of the mother with Rh incompatible blood transfusions has been found. Sensitization, once established, seems to persist for the remainder of one's life.

Attempts at prophylaxis by injections of hapten, an antigenic Rh preparation, allegedly capable of neutralizing the antibodies in the mother without stimulating their further production, proved futile. More recently, administration of ACTH and/or cortisone has been recommended during pregnancy as a means of preventing the disease. These substances are supposed to inhibit the production of antibodies. Although no such lowering of antibodies has been noted, some writers have reported prevention of the disease if these drugs were administered during pregnancy. It is possible that ACTH and cortisone prevent the union of the antigen with the antibody, as reported by this writer in connection with acquired hemolytic anemia of adults[11]. The reports on the efficacy of this pre-

ventive measure are contradictory. Apparently, prophylaxis of hemolytic disease of the newborn is still ahead of us.

Fetal erythroblastosis caused by ABO blood groups. Differences in ABO blood grouping between husband and wife, and between fetuses and their mothers are quite common. They occur in approximately thirty-five per cent of all pregnancies. In spite of this, the disease is much less frequently caused by these factors than by Rh incompatibility. Various reasons have been offered to explain the difference. According to some, from five to ten per cent of all cases of hemolytic disease of the newborn are caused by ABO incompatibility. Such pregnancies are called heterospecific pregnancies, and are defined as pregnancies in which the fetus contains a factor to which the mother may be sensitized. One of the reasons, why it is difficult to establish the relation of ABO factor incompatibility to the disease, is that antibodies against factors A and B are present naturally and their increase during pregnancy is observed regularly without any apparent disease of the newborn. Furthermore, even so-called "immune" antibodies are seen frequently during pregnancy, again without any relation to the condition of the newborn. On the other hand, cases of the disease with all classical findings, including fatal outcome, have been found in carefully studied instances without any explanation, except the presence of high titers of immune anti-A or anti-B isoagglutinins in the mother. It is interesting that the disease occurs not infrequently in first-born infants, and that the repetition of the disease in subsequent pregnancies, as seen in Rh incompatibility, is much less frequently observed in allegedly ABO hemolytic disease of the newborn.

Infants afflicted with this form of the disease should be treated as energetically with exchange transfusions as those with the disease due to Rh incompatibility. The selection of blood is based on a similar principle; it should not contain the blood factor which was the basis of heterospecificity between the fetus and the mother. The best blood is, as a rule, properly selected blood of group O.

For various other aspects of the Rh factor and of its clinical applications, the reader is referred to the previous publication in this journal[10].

OTHER BLOOD GROUP FACTORS

Since the discovery of the Rh factor, several other blood factors have been discovered. Two of the reasons for this increasing frequency of detection of new blood group factors are the more prevalent use of transfusions, due to greater availability of blood in blood banks, and the advances of surgery, which are followed by greater losses of blood and necessitate administration of larger volumes preceding, during and after operations. Another reason is the improvement of methods for the detection of incompatibilities. The result is that during the last ten years, an ever increasing number of new blood factors has been discovered, some of them responsible for transfusion reactions and some for hemolytic disease of the newborn. *Table* 6 lists most of the blood group systems that have been discovered until now. It also includes the incrimination of some of them for either transfusion reactions or fetal erythroblastosis.

The P system. In 1927, at the same time that they discovered the M and N factors, Landsteiner and Levine also discovered factor P. After absorption of the

Table 6

Nine Main Blood Group Systems

System	Antigens that have caused erythroblastosis fetalis and may cause hemolytic transfusion reactions
ABO	A, B
Rh	rh^1 (C)* hr^1 (c)* Rh_o (D)* rh'' (E)*
MNS	s
Kell	K, k
Duffy	Fy^a, Fy^b (F, f)
Kidd	Jk^a (Jk^b)
P	
Lewis	
Lutheran	
Private factors Examples	Be, Ca, Tj^a

*For the various type of the factors see (10)

species agglutinins, sera of certain rabbits, immunized with human red blood cells, agglutinated some samples of blood and did not react with others. This discovery added a new system to the two previously described. These blood factors were designated as P+ and P—. The same antibody entity was soon found in the serum of human beings and in normal, non-immune sera from horses, pigs, rabbits and cattle. The factor P+ is found in approximately seventy-four per cent of Caucasoids, and P— is found in the remaining twenty-six per cent; in Negroes, P+ is seen more frequently (ninety-seven per cent).

The P system is independent of the ABO and MN antigens. Occasionally, anti-P may increase after transfusion of P-positive blood. The antibody is, as a rule, active only at low temperatures, but in a few reported cases it was also weakly active at body temperature. In about one-fifth of all transfusions, P-positive blood is given to P-negative people. The fact that antibodies do not develop frequently, indicates that P must be a poor antigen. It has never been found responsible for hemolytic transfusion reactions.

The S system. A new factor, labeled as S, was discovered in 1947 by Walsh and Montgomery[13]. In contrast with the other blood sytems, S is associated with M and N; the new antibody is known as anti-S. There is no relation between the S factor and ABO, P, Rh or other blood types. It can be associated with M as M+, S+ (in nineteen per cent of the population); associated with MN as MN+, S+ (in thirty per cent of the population); or associated with N as N+, S+ (in eighty per cent). The absence of the S factor is designated as S, or as S—. The incidence of M+, S— is seven per cent, of MN+, S— twenty per cent, of N+, S— sixteen per cent.

The Duffy system. In 1950, Cutbush, Mollison and Parkin discovered the Duffy factor in a man suffering from hemophilia, who had had several blood transfusions during the previous twenty years[14]. The Duffy factor is found in sixty-five per cent of the population, and is designated as Fy^a and Fy^b (heterozygous) and Fy^aFy^b (homozygous).

The factor can be best detected by means of the indirect antiglobulin test, to be described later. Recently, this factor has also been detected by other methods.

The antigenicity of this factor is quite low, inasmuch as Duffy-positive blood is given to Duffy-negative patients in approximately twenty-three per cent of all transfusions, and reactions are relatively rare. Anti-Duffy natural antibodies have only been reported in one case.

The Lutheran system. The Lutheran system was described by Callender and Race in 1946[15]. Two phenotypes are recognized, Lu(a+) and Lu(a—); the genes and antigens are called Lu^a and Lu^b. At the present time, Lu^b can only be recognized by the absence of Lu^a; no anti-Lu^b serum has been found. The Lutheran factor, Lu^a, is present in about eighty per cent of the British population. The hypothetical Lu^b is present in about ninety-two per cent. Testing for the Lutheran factor is done similarly to Rh testing.

The Lewis system. The Lewis system was discovered in 1946 by Mourant[16]. As in other blood group systems, except S, the Lewis factor is entirely independent of other blood groups. A considerable number of sera with the anti-Lewis factor have been found. It is interesting to note that the Lewis antigen is more frequently detectable in infants than in adults. Practically all Lewis positives are also salivary non-secretors of AB. Two Lewis genes are recognized, Le^a and Le^b, and the genotypes are Le^aLe^a, Le^aLe^b, and Le^bLe^b.

The factor Le(a+) is present in from twenty-two to twenty-five per cent of the white population, and Le(a—) is present in from seventy-five to seventy-eight per-cent. The average is twenty-two per cent for the former and seventy-eight per cent for the latter. Pratically all ABO secretors are Le(a—). The Lewis system has been found responsible for hemolytic transfusion reactions in a few cases.

The Kell system. The Kell system was discovered in 1946 by Coombs, Mourant and Race[17]. The antibody was found in the sensitized mother of a child with

Table 7

"PRIVATE" BLOOD FACTORS[1]

Name	Antigen +[2]	Antigen -[3]	Antibody Titer	Antibody Technic Used	Origin	Antigenic Stimulus
Levay (1946)	3/7	350	1:20	Saline agglutinin	Immune?	Transfusion
Gr. (1946)	5/8	191	1:32	Saline agglutinin	Natural	None
Jobbins (1947)	2/4	120	1:1024	Indirect anti-globulin test	Immune	Pregnancy
Miltenberger (1951)	4/9	320	1:16-32	Indirect anti-globulin test	Immune	Pregnancy
Jay (1951).	6/8	1500[4]	1:8	Hemolysin	Immune	Gastric tumor
(1952)	0/1	112[4]	1:128	Saline agglutinin	Immune?	Pregnancy?
Berrens (1952)	5/9	574	1:512	Serum-albumin, indirect antiglobulin test, enzyme-treated RBC	Immune	Transfusion and pregnancy

[1]Based in part on table by P. Levine (Tr. New York Acad. Med. Sc. II, 13: 205-209, 1951).
[2]Number of specimens positive out of total tested in the family.
[3]Number of negative (or positive) specimens in the random population.
[4]Random samples of population positive.

hemolytic disease of the newborn. In another case, observed by Wiener, the antibody, anti-Kell, was responsible for a severe hemolytic transfusion reaction.

The Kell blood factor is found in ten per cent of the population; ninety per cent of the population is Kell-negative.

Family blood factors. In addition to the previously listed blood factors, present in various percentages in the general population, blood factors present only in members of a single family or generally prevalent but absent only in members of a single family, have been described. *Table* 7 lists most of these recently discovered so-called "family" blood factors, but an ever-increasing number is being published at frequent intervals. A more detailed account of the family blood factor discovered by our laboratory, is typical of those discovered by others[18].

Soon after birth, a woman's second child developed typical findings of fetal erythroblastosis. Examination revealed that the mother was B, Rh-positive; the husband B, Rh-negative; and the child B, Rh-positive. The mother had an antibody, which reacted only with the blood of the husband and four other of his blood relatives. Several hundred other persons were tested and none of them had the new blood factor. As is customary in these cases, the blood factor was labeled with the family name, Berrens. The history revealed that the woman had been transfused with the husband's blood after the birth of their first child. This transfusion and the second pregnancy were sufficient to sensitize her and to produce the antibodies. The first pregnancy was not responsible for the sensitization because the first child was Berrens-negative.

Other such reports indicate that a husband's blood, even if found compatible by the accepted methods of testing, should never be used in a transfusion for his wife. This prohibition also affects his blood relatives, including his children. In this particular case, however, the nature of the incompatibility would not have been discovered if the husband's blood had not been tested. This suggests that the husband's blood and, if possible, also the child's blood, should be used in testing for antibodies in the blood of a woman giving birth to a child with hemolytic disease of the newborn.

One cannot fail being impressed by the rapidly increasing number of newly detected blood factors and it is reasonable to hope that the time will eventually

Table 8

INHERITANCE OF ABO FACTORS

I. Law of Inheritance

Parent A can transmit only A or O (O = absence of A)

Parent B can transmit only B or O (O = absence of B)

hence

A and B cannot be present in the blood of a child unless present in the blood of one or both parents.

II. Law of Inheritance

Parent AB must transmit to child A or B

hence

Person AB cannot be parent of child of group O (because O denotes absence of A and B)

III. Law of Inheritance

Parent O can transmit to child only O, but not A or B

hence

Person O cannot be parent of child of group AB.

come when every person will have his own individual blood formula.

MEDICOLEGAL APPLICATION

Application of blood groups to questions of paternity. The ABO, MN, Rh and other blood group factors are inherited as Mendelian dominants. This is the basis for their application in cases of paternity lawsuits. Usually the question revolves around a woman's claims that a certain man is the father of her child, and the man's denial of paternity. Sometimes, the problem presented is an alleged mixup of newborn infants in hospitals.

In the case of the ABO factors, certain rules have been established which can be used in such problems (*Table* 8). Applying the rules to the results of blood group testing in the mother, the child and the alleged father, it is possible to exclude approximately one out of six innocently accused persons. Failing to exclude paternity does not imply that the individual is the father of the child, but merely states that he may be. A similar number of exclusions is possible by the application of the M and N factors to the problem. The rules governing the inheritance of the M and N factors and their application to exclusion of paternity are reproduced in *Table* 9. The rules of inheritance governing the Rh factor are similarly applicable. The inheritance of the other blood factors is also being studied. The chances of exclusion are greater if the alleged father belongs to the rarer, rather than the more common blood groups. For example, a man belonging to blood group AB, Rh-negative has a much better chance of being excluded, if innocently accused, than if his blood formula were A, Rh-positive.

Application of blood groups to identification of stains. In criminal proceedings, the question of identification of blood stains, or of stains caused by other secretions, may be indicated. Such problems arise when, for example, a defendant claims that a stain on his clothing is the result of his own nosebleed, or that it is a blood stain of an animal (a chicken, a rabbit, etc.). Under favorable circumstances, the blood group of such stains can be identified. The ABO blood factors are most reliably identified. Demonstrating that the stain contains blood and not a dye, and that the blood is human, is relatively easy.

The blood grouping of stains caused by semen may also be determined in some instances, since sperm contain blood group factors in a rather strong concentration.

In the case of stains, blood and sperm alike, the blood group is determined by adding extracts of these stains to sera containing isoagglutinins. Neutralization of the isoagglutinins, determined by titration, helps to identify the blood group.

Dried up saliva, as on cigarette stubs or gummed surfaces of envelopes or stamps, can also be tested for blood groups.

For details regarding the medicolegal application of blood groups, the reader is referred to a recent exhaustive report by a special committee of the American Medical Association[19].

Table 9

INHERITANCE OF MN FACTORS

Parent M must transmit factor M to his child.

Parent N must transmit factor N to his child.

hence

IV. Law of Inheritance

M and N cannot appear in a child unless present in one or both parents.

V. Law of Inheritance

Parent M cannot have child N.

VI. Law of Inheritance

Parent N cannot have child M.

SUMMARY

The study of blood groups has been applied to many branches of medicine and to disciplines outside of the field of medicine. These include:

(1) Surgery (blood transfusions).

(2) Obstetrics.

(3) Pediatrics (hemolytic disease of the newborn and kernicterus).

(4) Neurology (kernicterus and possibly other forms of mental retardation in the young).

(5) Pathology (fetal erythroblastosis).

(6) Serology (new techniques of antibody determination).

(7) Legal medicine (exclusion of paternity and identification of stains).

(8) Hematology (The discovery of so-called "incomplete" antibodies has revolutionized the study of various diseases of the blood, especially of acquired hemolytic anemia).

(9) Study of inheritance of human disease.

(10) Clinical pathology and blood banking.

(11) Anthropology (variations in the distribution of blood group factors in various races).

(12) Genetics (inheritance of the blood factors).

(13) Comparative zoology and evolution (presence of blood group antigens in various species).

It is reasonable to assume that there are abundant opportunities for research in this field and that many important areas remain unexplored.

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AMYOTROPHIC LATERAL SCLEROSIS

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INTRODUCTION

Amyotrophic lateral sclerosis is a disease of middle life, progressive in course, and characterized by upper and lower motor neuron pathology. It is sporadic in incidence and until recently without any clear cut hereditary background. Since its original description by Charcot, the concept of this condition has broadened to include other entities, such as the spinal types of progressive muscular atrophy (infantile and adult forms), progressive bulbar palsy, and lateral sclerosis. These diseases are all of similar pathology differing clinically only in the groups of muscles affected and the degree of spasticity, atrophy, and progression.

HISTORY

Charcot, in 1865, first described and named the condition. He stressed the difference between this syndrome and the progressive muscular atrophy of Aran and Duchenne. In 1861, Duchenne described progressive bulbar palsy in detail. Dejerine, in 1883, showed the relationship of progressive bulbar palsy to amyotrophic lateral sclerosis. Kahler and Pick, in 1879, called attention to the gross motor convolutional atrophy that sometimes occurs, and Kojewnikoff was the first to trace the degeneration of pyramidal fibers from the motor cortex into the internal capsule and brain stem. Spiller, Bertrand and van Bogaert, however, were unable to trace the degeneration higher than the brain stem in other cases.

ETIOLOGY

The etiology is unknown but there are many theories.

(1.) *Stress* may be a contributing factor; this includes disturbed emotional states, exposure to cold, and other types.

(2.) *Nutrition* may also be a contributing factor. Koerner studied the high incidence of amyotrophic lateral sclerosis on Guam and noted that many of the natives showed signs of under-nutrition and avitaminosis.

Ask-Upsmark described five cases of the disease following gastric resection and considered that the disease might be due to deficiencies with neurologic manifestations similar to those seen in pernicious anemia. Wechsler and others believe Vitamin E deficiency is an important factor.

(3.) *Trauma* to the spinal cord has been related to the onset of amyotrophic lateral sclerosis. The disease has been reported in pneumatic hammer operators and following other types of trauma. Pollock, reviewing this subject, does not feel that trauma is an etiological agent. Electric shock may produce spinal cord changes resulting in a clinical picture of amyotrophic lateral sclerosis.

(4.) *Inflammations*: The disease has been related to lues and encephalitis as well as to other viral and bacterial infections.

(5.) *Vascular disturbances* have been implicated by some. Koerner's cases showed an incidence of clinical arteriosclerosis of seventy per cent and an incidence of minimal hypertension of thirty-three per cent.

(6.) *Abiotrophy*: Gowers and Spiller believe that the disease may be due to lack of cellular potentialities, causing the neuron to degenerate permanently.

(7.) *Heredity*: In Koerner's series, forty per cent of patients had a history of the disease in their immediate families; however, this has not been a prominent finding in any other series.

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(8.) *Toxins*: The disease has been described following exposure to lead, other heavy metals, and certain gases.

(9.) *Metabolic*: Reports have described amyotrophic lateral sclerosis in association with acromegaly and with progressive lipodystrophy. Such associations may be coincidental.

(10.) *Allergy*: Some authors believe there is an allergic component to the disease.

INCIDENCE

The disease usually occurs between the fourth and sixth decades. The average age of onset in a large series was forty-seven, and the range was from fourteen to eighty-nine years, with over eighty per cent between forty-one and sixty-five years of age. The disease constitutes about three per cent of *neurologic* admissions; 150 cases were seen at the Mayo Clinic in a five-year period. The ratio of males to females lies between 2:1 and 4:1. There does not seem to be any statistical relationship with race, occupation, economic status, or climate. There is also little relationship to malformations and anomalies, and heredity ordinarily seems to play no part, although familial forms have been reported. The frequency of such cases is not great enough to class amyotrophic lateral sclerosis with the hereditary or familial diseases.

Recently, Koerner has reported an unusual series of cases occurring on Guam, which is of considerable interest. The island has two separate hospitals, one for natives and one for personnel of the United States Government. In reviewing over 13,000 admissions to each hospital, he discovered forty-six cases among the natives, and two among the United States Naval Hospital admissions. Both of these patients were Guamanians inducted into the United States Army. Among the natives, forty per cent of the cases had a history of the disease in some member of their family. None of the neighboring islands has a similar incidence. The people of Guam are predominently of mixed Spanish and Filipino blood. Many of them suffered from intestinal parasites and the effects of malnutrition during enemy occupation during World War II.

Duration: The average duration of the spinal form is twenty-two and four-tenths months with a range of eight to forty-one months. Patients with bulbar symptoms live an average of thirteen months from the onset of their illness with a range of three to thirty-five months. Some victims live as long as ten years from the onset of symptoms.

CLINICAL SYNDROMES

As the disease proceeds to involve the upper and lower motor neurons, clinical signs depend upon that portion of the nervous system affected. The upper and lower motor neurons may not be affected simultaneously or to an equal degree. This results in diverse clinical pictures with varying degrees of atrophy, spasticity, and progression.

(a.) *Lateral sclerosis*: This is a syndrome of progressive pyramidal tract disease with spastic weakness, hyperactive deep reflexes, positive Babinski signs, and absent abdominal reflexes. The symptoms of pseudobulbar palsy may also be present. Erb, in 1877, first called attention to this condition. In his cases, pathological changes were found in other parts of the spinal cord, including the cerebellar tracts and tracts of Goll. Spiller studied eight cases, six of which showed evidence of anterior horn cell degeneration at autopsy. It therefore seems unlikely that primary lateral sclerosis exists as a separate entity, although in exceptional cases there may be a relatively inconspicuous degeneration of the anterior horn cells.

(b.) *Bulbar forms*: Bulbar symptoms may occasionally develop initially. There may be difficulty clearing the throat, shortness of breath, disturbances in enunciation, and regurgitation of food. Later, the patient may be unable to hold his breath, blow out a match, or swallow well. Speech may become inarticulate, and disturbances of the eye muscles, as well

as paralysis of the jaw and lower facial muscles have been reported. If the lower motor neurons are chiefly affected, the signs are those of bulbar palsy with atrophy; while if the cortical bulbar tracts of the cerebral hemisphere degenerate, a pseudobulbar palsy will appear with no atrophy of the tongue, or other paralyzed muscles. The jaw jerk is increased. Emotional over-reaction is noted; the emotional response may be unusually prolonged or may be inappropriate, supposedly due to the release of the thalamic and other centers from cortical control. The symptoms of the two varieties are sometimes mixed. Fasio and Londe have described the bulbar form in infants with a rapidly fatal course.

Ophthalmoplegic forms have been reported, although it is questionable whether this is an amyotrophic lateral sclerosis analogue. The majority of these cases have an early onset or are heredito-familial. Von Graefe, in 1868, called attention to this condition. Only the external ocular muscles are involved. Ptosis is one of the earliest symptoms, followed by slow spread to the other external ocular muscles.

(c.) *Progressive muscular atrophy (of Aran and Duchenne)*: When the pathological changes are predominently in the ventral horns, this type of clinical picture is produced. The onset is gradual and fibrillations and fasciculations of the muscles of the hand and forearms, as well as those of the shoulder girdle, may be noted, associated with weakness and atrophy in these parts. The atrophy begins in the small muscles of the hands and gradually involves the forearms and shoulders. "Winged" scapulae may be prominent. The deep reflexes are ultimately lost in the paralyzed limb, with flaccid paralysis. Electrical changes progressing to a reaction of degeneration are produced. The disorder may extend to the lower extremities, as well as to the bulbar muscles, and the clinical picture depends on the proportion of involvement of upper and lower motor neurons. Familial forms do occur and are usually associated with foot deformities such as pes cavus, equinovarus, or hammer toe.

(d.) *Infantile progressive muscular atrophy (Werdnig-Hoffman)*: This distinct term is applied because the condition develops between the age of six months and one year and has a strong familial character. The lower motor neurons are often involved almost exclusively, and the syndrome is rare. The atrophy is more or less symmetrical, often involving the hips and lower extremities first and then the shoulders and back muscles. Flaccidity gradually progresses until death supervenes, usually within five years.

(e.) *Amyotrophic lateral sclerosis (form of Charcot)*: As mentioned, this condition represents a combination of upper and lower neuron disease showing mixed atrophy and spasticity, as well as hypo- and hyperactive reflexes.

(1.) Onset and early stage: The condition may begin with a dull aching in the muscles and cramps and paresthesias may occur; there may be awkwardness in the fingers and stiffness in the legs. A common complaint is muscle weakness, especially in the trunk, extremities, head, and neck. Fasciculation is also common early.

Although the disease may begin in any portion of the spinal cord or brain, in one large series compiled by Friedman and Freedman, thirty-eight per cent first complained of lower extremity difficulty and thirty-one per cent of upper extremity difficulty, while twenty-one per cent presented bulbar symptoms; the remainder offered mixed complaints. It is usually reported that the upper extremities and the bulb are the primary sites of early symptoms. Characteristically, the upper extremities show atrophy and

flaccidity, while the lower limbs show spasticity.

(2.) Signs of lower motor neuron involvement: These signs include muscle atrophy with weakness or paralysis, fasciculations, and diminished reflexes. The early signs of wasting may appear in the interossei and lumbricales of the hand. As atrophy of the hand muscles becomes more complete, the thumb recedes dorsally to fall in line with the fingers giving the appearance of a *simian hand.* When spasticity is present the appearance may be that of a *claw hand.* When atrophy is virtually total and the flexor tendons of the hand stand out, one may see the picture of the *cadaveric hand.* The upper arm and shoulder girdle are next most frequently involved, while atrophy of the legs may appear late. As the condition spreads, the muscles of the tongue, palate and pharynx are commonly affected. Although there may not be visible muscle wasting, muscle weakness is proportional to atrophy. Fibrillations and fasciculations are highly characteristic, widespread, and precede muscle wasting. The reflexes become diminished or absent in the wasting muscle, but may occasionally be intact even with extensive atrophy, due to the presence of unaffected fibers scattered among the atrophic ones. Ninety-six to ninety-eight per cent of clinical and autopsy cases show some signs of anterior horn cell change.

(3.) Signs of pyramidal tract involvement: When the corticospinal tracts are involved there are hyperactive tendon jerks, hypertonus, loss of abdominal reflexes, and plantar extensor response. In one series, twenty-five per cent of the patients showed no clinical signs of pyramidal tract disease. Perhaps the pyramidal signs are somewhat obscured by advancing muscle atrophy; the absence of clinical evidence of pyramidal tract disease does not mean that there is no pathology in the lateral columns. Lassek and Evans have shown that the Betz cells account for only three per cent of the large myelinated fibers in the pyramids. Most of the finer fibers and some of the unmyelinated fibers arise from the frontal cortex, rostral to area four, and may also arise from the area superior to the central fissure. In some cases, the evidence of corticospinal tract disease cannot be traced higher than the pons or medulla. There is some confusion as to the relation of pyramidal tract signs to corticospinal tract disease. It is possible that the only clinical signs implicating the p y r a m i d a l tracts may be the impairment of skilled or fine movements. Other signs, such as spasticity and increased tendon reflexes, may depend on the remaining functional c o r t i c a l efferent halves and the tracts of the lenticular system. Evidence of corticospinal tract involvement has been found at autopsy in a number of cases where there was no clinical evidence of this.

(4.) Sensory disturbances: Subjective sensory disturbances such as muscle aches and cramps, etc., may be present at one time or another in fifty per cent of the patients. Objective sensory findings, disturbances of pain or touch, and sometimes of vibration, are found in about ten per cent.

(5.) Sphincter disturbances: Difficult initiation of urination may be found in about fifteen per cent of the cases.

(6.) Bulbar symptoms: There may be explosive laughing or cry-

ing, unaccompanied by genuine emotion, as well as neurosis or psychosis. Many observers feel that the mental picture is dependent on the specific personality structure of the individual, rather than any specific determinant of the disease itself, or may be a reaction to a chronic incapacitating disease. The psychosis, however, may be related to the degenerative process; Kesert and Friedlander have presented a case that may fit into this category.

(7.) Atypical cases: Hemiplegic, monoplegic, tetraplegic, and proximal forms have been observed. Extrapyramidal signs have been reported.

CLINICAL PATHOLOGY

The spinal fluid is normal in most cases, but there may occasionally be a slight increase in protein or sugar. Metabolic studies are inconclusive and show no consistent abnormalities. A few of Koerner's cases on Guam had anemia and eosinophilia, common among parasite infested populations.

PATHOLOGY

Spinal Cord: The anterior horn cells of the spinal cord appear smaller than normal and the anterior roots are often wasted, with degeneration of the ganglion cells. These findings are often most marked in the cervical enlargement as well as in the lumbar enlargement, falling off somewhat in between these levels. The changes are very often widespread and their severity is not always proportional to the clinical condition. The ganglion cells may exhibit chromatolysis, the neurofibrils disappear, and often there is a granular deposit of lipochrome. The number of cells is reduced and there is slight secondary gliosis and perivascular round cell infiltration. There is degeneration of the white matter of the spinal cord, most marked in, and often confined to, the antero-lateral columns. Pyramidal fibers, both the direct and the crossed, suffer most; this degeneration is never equally severe at all levels. The spinocerebellar tracts may show degeneration. The rubrospinal, vestibulospinal, and tectospinal tracts may be variably degenerated.

Medulla: Ganglion cells of the medullary motor nuclei show degenerative changes, especially the hypoglossal nucleus, the dorsal nucleus of the vagus, the nucleus ambiguus, and the trigeminal motor nucleus. The facial nucleus is less severely affected; some changes have been seen in the facial sensory nucleus. The third and fourth nerve nuclei usually escape damage. There is a marked degeneration in the medullary pyramids; involvement of other tracts has been described.

Cerebrum: Slight atrophy of the ascending frontal convolution has been described; microscopic changes are most marked in the cortex anterior to the fissure of Rolando. There may be a loss of Betz cells with dissolution of Nissl substance. The typical lesion in subacute cases shows lipochrome degeneration of the ganglion cells in the frontal and precentral areas, most marked in the third and fifth cortical areas. Similar changes with slight glial overgrowth may be found in the middle third of the corpus callosum and the posterior limb of the internal capsule.

Peripheral Nerves and Muscles: The anterior roots and perpheral nerves show degeneration and atrophy of the myelin sheaths; the muscles supplied by the diseased nerve cells show atrophy of contractile substance with increase in sarcolemmal nuclei and fatty infiltration.

THERAPY

Vitamin E, trypan red, Tolserol (mephenesin) and adrenal cortical extract have all been claimed to be useful. However, there is no agent known to be of definite value. The palliative, supportive and physical therapies indicated by the type of the motor impairment found in any individual case are implicit in the management of these patients.

DIFFERENTIAL DIAGNOSIS

The disease must be distinguished from other diseases involving the spinal cord and bulb, and from other conditions with muscular wasting.

(1.) *Syringomyelia* is distinguished by its occurrence earlier in life, a sensory segmental loss of pain and temperature, and the presence of trophic disturbances such as scoliosis and pectoral hypertrophy. Fasciculation is seldom present.

(2.) *Subacute combined degeneration* runs a subacute course with paresthesias of the distal parts of the extremities progressing to ataxic paraplegia. The presence of marked posterior column signs, with macrocytic anemia and achlorhydria, helps to differentiate this condition.

(3.) *Cervical cord tumor or cervical spondylosis (discs)* usually show pain accompanying upper limb weakness and eventually produce atrophy, as well as a sensory level and bladder disturbances. Later there is subarachnoid block and increased spinal fluid protein.

(4.) According to Temple Fay, some cases resembling amyotrophic lateral sclerosis are due to *compression of the upper cervical cord* by enlarged epidural veins or venous sinuses, which can be surgically compressed.

(5.) *Syphilitic meningomyelitis* shows weakness and wasting, accompanied by severe radicular pain; signs of pyramidal degeneration are usually absent; pupil abnormalities, as well as paresthesias and positive serology may be present.

(6.) *Muscular dystrophies* usually develop at an early age, and the atrophy is proximal rather than distal. Usually, there is lack of fibrillation or pyramidal tract involvement.

(7.) *Myotonia atrophica* has a peculiar distribution of wasting, with predilection for the sternocleidomastoid and quadriceps muscles. There is myotonia, absence of fibrillation, and a personal or familial history of cataract.

(8.) *Cervical rib* shows small muscle wasting that is limited and not global, as well as sensory, and sometimes, vascular disturbances. X-rays are helpful. There is no fibrillation and pain is usually felt along the ulnar margin of the hand and forearm.

(9.) *Radiculitis* causes atrophy of the muscles supplied by the affected root. The fifth cervical nerve is most often affected. The onset is acute and is associated with much pain in the neck and shoulder. The condition is not progressive and gradually improves.

(10.) *Scalenus anticus syndrome* may produce a picture similar to that of cervical rib.

(11.) *Peroneal muscular atrophy* has a peculiar distribution which begins in the periphery of the limbs and is associated with sensory loss. The disease is usually familial and often appears in childhood.

(12.) *Arthritis of the hands and fingers* may lead to wasting of the hand muscles. Joint pain, swelling, and limitation of motion, or a history of such, are valuable in differentiating the condition.

(13.) *Pseudobulbar palsy* may occur from vascular lesions or infections, etc. If the onset is sudden, the condition is not likely to be confused; if it is insidious, the absence of atrophy and the presence of signs of arterial degeneration may help to differentiate this condition.

(14.) *Bulbar palsies and polio* are more abrupt in onset and occur with general toxic symptoms.

(15.) *Myasthenia gravis* starts at an earlier age and has no atrophy or fibrillation, is relieved by rest and responds to prostigmine.

(16.) *Atrophies of disuse* do not exhibit fibrillary twitching, or electrical irritability, and there is no paralysis.

(17.) *Reflex atrophies* are often seen about arthritic joints and are severe and rapid in onset. They are associated with cyanosis and coldness of the extremities.

(18.) *Injuries of the spinal cord* are characterized by sudden onset, paresis, bladder disturbances, sensory symptoms, muscle atrophy, and pain.

(19.) *Other conditions* that may require differentiation are toxic myelopathy, progressive hypertrophic interstitial polyneuritis of Dejerine-Sottas, Erb's primary atrophic myopathy, Landouzy and Dejerine's facio-scapulo-humeral type of myopathy, thyrotoxic myopathy, multiple sclerosis, and islet cell tumor of the pancreas with profound paroxysmal hypoglycemia.

(Continued on page 42)

THE SOCIO-ECONOMIC COSTS OF ILLNESS*

("The Social Horizons of Preventive Medicine and Public Health")

H. ELISHEWITZ, Ph.D.**

The social and economic implications of any disease are as important as any other phase of the disease. Because the student and the practicing physician are too little aware of this fact, it must be emphasized and reiterated. The borderlines of medicine impinge not only upon the domains of the physical, chemical, and biological scientists, but also upon the fields of the sociologist, the economist, the political scientist and the philosopher.

The role and responsibility of the physician are as germane and as important as the role and responsibility of the other specialists in many medico-social problems. Consider for a few moments, if you will, the significance and ramifications of the following:

> "Science finds out ingenious ways to kill
> Strong Men, and keep alive the weak and ill—
> That these a sickly progeny may breed,
> Too poor to tax, too numerous to feed." * * *

Dare the physician neglect not only his duty as a healer of the infirm, but also his responsibility to society in other medical and paramedical charges, *viz.*, to minister to the needs of, and to *maintain* the health of, the community and its members? It is in these paramedical phases that the physician encroaches upon the fields of the sociologist, the economist, *et al.* He does so today, but in the society of the future, responsibilities and functions will become more and more interminably intertwined.

The field of Public Health has been defined as the "application of the science of preventive medicine through civil government for social ends." Can borders be drawn between medicine and preventive medicine, between preventive medicine and public health? The impracticability of drawing a line between the border fields of medicine and social welfare is evinced by the tendencies of the Departments or Ministries of Health to be called, in most countries, by some variation of the term, "Ministry of Health and Social Assistance or Public Welfare." Even here in the United States, the recently created cabinet post in the federal government is entitled, "Department of Health, Education, and Welfare."

The field encompassed by the title of this paper, is tremendously large and complex. It, by definition, includes such far-ranging problems as support and payment for medical care, the financing of medical research and education, nutritional and housing requirements and status of communities, problems of geriatrics, and even the subjects of "lebensraum" and conflict. Because of the limitations of time and space, the discussion here will be limited to three phases:

1. The spectrum of disease.
2. The economics of illness.
3. The sociology of illness.

1. THE SPECTRUM OF DISEASE. (*A Contribution to a Definition of the Term, "Disease"*).

The currently accepted and used definitions and concepts of the term "disease" are inadequate for the needs of modern medicine. We cannot any longer accept the average dictionary definition of disease as: "an illness, malady, ailment or sickness;" "an alteration or disturbance in function or structure of any organ or part of the body interrupting or disturbing the performance of its vital functions;" "a definite morbid process having a characteristic train of symptoms;" "an interruption or perversion or an abnormal state of function of any of the organs, or tissues, or body as a

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*** Anonymous, "LONDON SPECTATOR," 1929.

whole;" or "deviation from the standard of health in any of the functions of the body."

All these definitions have one thing in common. They are restricted and refer only to objective signs of disfunction as seen in the afflicted individual. They refer to the symptoms which, with its accompanying progression of functional and structural changes (pathology), constitute the clinical picture.

The cataloguing of the symptoms and the statement of the clinical picture of disease *do not constitute* a definition of disease. This delineation of objective signs of disfunction is merely the *"WHAT"* of disease. The *"WHERE,"* the *"WHEN,"* the *"HOW,"* the *"WHY,"* and the *"HOW MUCH,"* of disease are every bit as important as this *"WHAT."*

Contrary and antithetical to the commonly accepted definition of the term, disease is a complex multiple phenomenon. The resulting disturbance in structure or function is only one phase, the clinical manifestations or the "what," of a disease. Disease itself includes all the multiferous ramifications of how and why the clinical manifestations were brought about as well as all its other associated phases.

We may best picture any disease as a beam of white light entering a prism or spectral grating and being dispersed into the elemental spectral colors (*Fig.* 1), each color representing one component phase of the disease.

These phases,—etiology, relationships, nomenclature, incidence, geographical distribution, epidemiology, morphology, biology and life-cycle of the pathogen, immunity, pathogenesis, pathology, symptomatology, complications and sequelae, diagnoses and differential diagnosis, therapy, prognosis, prophylaxis, history, and social and economic implications—all have claim to being important components of a disease. No one phase can be singled out and stated to be "the disease." Each phase grades imperceptibly into the other phases on either side of it. Disease, thus, is a spectrum or a continuum—not an isolated or sharply defined facet of a clinical syndrome alone.*

As shown in *Fig.* 1, the clinical pic-

Figure 1

ture of disease which is commonly referred to as the "disease," only constitutes the "what" of the disease. The other phases, suitably grouped, constitue the "where," the "why," and the "how," the "when," and the "how much."

Quain[1] in 1894, clearly set forth some of these ideas, but the integrating character of this analysis is frequently forgotten.

Much of this discussion on definition of disease is to stress the point that, as shown in *Fig.* 1, the social and economic implications of a disease are as important as the clinical picture. The physician usually loses sight of these considerations. In analyzing a disease, the physician will usually give thought to the etiology and the method of contact as well as the clinical phases, but he rarely thinks of the social and economic phases.

2. THE ECONOMICS OF ILLNESS (*National Health as a National Resource*)

* It should be remembered that non-communicable diseases and those not caused by infectious agents also have an epidemiology which may be analyzed by appropriate techniques, and in most respects are directly comparable to the communicable diseases.

One of the foundation stones in current thinking in preventive medicine is that the human population of a country is a resource of that country more important than any other natural resource, and that the total value of that population resource is capable of analysis. The corollary of this concept is that the maintenance of the health of this resource is the economical utilization of the resource; illness, lost-working time, and death in the population is an economic waste, never to be recovered.

In the past, scant attention was paid to human population as a resource. The natural resources, the agricultural resources, the machinery resources could all be evaluated and analyzed. Human life, in many lands and at many times, did not count for much.

The standard of living of a population is in direct proportion to its productive capacity. Every lost-time illness or death due to disease means a lowering of that standard of living. Although complex, it is possible to calculate this loss in terms of dollars and cents.

A rough estimate of the economic losses due to illness may be obtained by the use of the following formula:

Incidence of disease	×	Lost-time due to illness	×	Productive capacity of individual worker	=	Economic Loss

Economic loss is expressed as wages, profits, or production. There are many possible ways of arriving at this figure; the most widely used one is to take the estimated total value of the annual production of all products and services produced by the labor of the country, and divide it by the man-days worked during the year (number of employed × working days in the year). A better, more nearly true method, and one which yields a much higher total loss, would be to take the total value of the production of the country, capitalize it at an average rate (say 7 or 8%), then divide by the total labor force. This gives the average value of the *investment* in human resources. Losses may then be calculated on the basis of the lost interest on this investment, rather than on the basis of lost salaries alone. [See Elishewitz (1946, 1953, 1954) for this type of analysis].

This yields the crude data from which can be calculated the tremendous lost-productivity of a nation. Because it does not take into account the innumerable complex modifying factors—medical, social, and economic—the figures cannot be more than rough estimates. The accuracy and completeness of the sickness surveys are of prime import in accumulating the basic data. The relative paucity of good modern data shows the need for more extensive and frequent surveys.

To cite an example based on one illness, recent studies showed a rate of three minor respiratory ailments per person per year, of which 50% of the people surveyed had at least one disabling (lost-time) attack per year[2]. By translating this into national terms, the tremendous import of the common cold in our national economy can be shown. About 62,000,000 people are gainfully employed in the U. S. A. If each of them loses an average of four days of work per year due to these illnesses, a total of 248,000,000 man-days are lost per year. The average wage in this country is about sixty dollars per week or ten dollars per working day. Thus the lost economic productivity is over 2,500,000,000 dollars per year in this country, due to the common cold alone. By adding the cost of professional and home medications to this figure we have a rough idea of what this disease is costing.

The population of this country is now 160,000,000. The economic loss given refers only to the laboring force, *i.e.*, the gainfully employed (roughly 40% of the total population). It does not take into account the costs of illness to the non-employed, who also contract the common cold just as frequently as the employed group.

Since current productivity in this country is considered to be about 365,000,000,000 dollars per year, the common cold can be considered to account for a loss of 0.7% of this amount.

Similar transpositions can be made from various detailed sickness surveys[2, 3]. However, they all suffer from the hazards of extrapolation. Winslow[4, 5]

cites many figures picked at random on the economic costs of various diseases in different areas of the world: *viz.*, that malaria causes an economic loss of 240,000,000 dollars per year in India; Schistosomiasis causes a loss of 60,000,000 dollars per year in Egypt; malaria and tuberculosis cause a loss of 660,000 dollars a year or an average per capita loss of thirty-three dollars per year. In the Philippines, male cases of paresis alone cause an estimated annual loss of income of 112,000,000 dollars in 1945 (Iskrant[4]), and although deaths from tuberculosis have been reduced to one-tenth of what they were a century ago, this disease still causes a loss to the U. S. A. of 1,000,000 years of future working life and 350,000,000 dollars per year for medical care and related services*.

Oscar Ewing[6], the former director of the Federal Security Agency, estimated that the annual cost of illness in the U. S. A. was 38,000,000,000 dollars per year itemized as follows:

Cost of premature death.....11,000,000,000 Dollars
Cost of total disability.....11,000,000,000 Dollars
Cost of partial disability....11,000,000,000 Dollars
Cost of short-term illness.. 5,000,000,000 Dollars

The figures presented here are, for the most part, only estimates. Detailed and more exact analyses of the economic losses have seldom been made because of the complexities of the many factors involved. Yet the strongest inducement to undertake remedial or preventive measures for practical-minded legislators and administrators is to show them in concrete terms the actual real cost of the illness to their economy.

Elishewitz[7] in 1946, by restricting the analysis to an industrial community in a single area which had a complete record of accurate statistics was able to develop principles on which such an analysis could be made. Calculating the costs of these losses, due to malaria, permitted the establishment of malaria control programs to be placed on an economically justifiable basis by the industry.

The analysis of the cost of malaria[7] showed that in one oil camp in eastern Venezuela, with 1400 employees and a malaria rate of 332 cases per 1000 employees per year (average from 1940-1946), this disease alone was costing the oil company almost 500,000 dollars per year, or 350 dollars per year per employee. Within two years after the introduction of the DDT-residual spraying control program, malaria was virtually eradicated from the area at a cost of about 25,000 dollars per year for the continuing operation[8,9,10,11] (a mere 5% of the previous gross annual cost of the disease).

The methods of analysis and equations developed lend themselves to wider use and are applicable to many other diseases. The following outline presents the factors which must be considered in determining the economic losses:

FACTORS INVOLVED IN ECONOMIC LOSSES IN INDUSTRIAL ILLNESS

I. Labor Costs

1. Lost wages during time off.
2. Decreased labor efficiency during incubation and convalescent periods.
3. Excess personnel maintained on payroll to offset the lost-time cases.
4. Cost of utilities, services, and camp-maintenance supplied to families of lost time cases and to excess personnel.

II. Hospitalization and Treatment Costs Attributable to Illness

1. Cost of drugs and medication.
2. Hospitalization costs:
   a. room and board charges.
   b. percentage of general hospital overhead and operating costs:
      I. staff and help salaries;
      II. maintenance and operation;
      III. depreciation on capital investments.
3. Clinic and dispensary expenses.

III. Costs of Conventional Control and Prevention Measures (depends on disease under consideration)

IV. Indefinable Costs

1. Lost profits and interest on:
   a. tools lying idle;

* The impact of these figures on the economy of the nation must be viewed against the standard of living, the total national production, and wage rate in each country. The figures are quoted in U.S.A. dollars; but in these and other undeveloped areas, the annual *per capita* income of the population averages only forty to sixty dollars compared to about 1,600 dollars here in the U.S.A.

b. job completion delays;

c. human resource investments.

2. Effect of employee morale.

Detailed considerations should also be given to one more important medico-economic factor in Public Health, *viz.*, the cost of premature death, i.e., the economic loss resulting to a community when an individual dies before reaching a productive age (the age at which he produces more than he consumes).

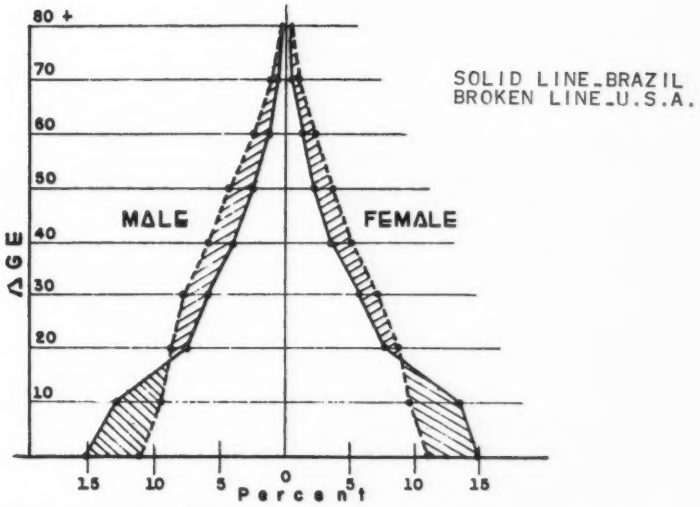
Hanlon[12,4] analyzed in detail the costs of rearing a child to maturity in the U. S. A.—or to the age of eighteen at which time he is considered capable of earning his own livelihood. Taking into consideration the costs of living, the health risks, the cost of child-birth, the rearing and education, the provision of recreational facilities, etc., Hanlon calculated that it costs 20,055 dollars to rear a child to the age of eighteen years. The net prospective earning power of the individual after the age of eighteen to a life-expectancy of sixty-five is 34,000 dollars above the cost of living for himself and his family. Thus, a child who dies before eighteen represents a net economic loss varying from 800 dollars (if death is in child-birth) to 20,000 dollars (if death is at the age of eighteen).

Campbell and Morehead[13] have carried this one step further and showed that premature death is an important factor in the economic under-development of Brazil and the other under-developed areas of the world. Life expectancy and age-distribution go hand-in-hand and are prime public health problems which are directly related to the productive capacity of that population. In Brazil with a population of 50,000,000 (1950) the infant mortality rate (deaths under one year of age/1000 population) is 180, in the U. S. A. it is 47; the tuberculosis death rate is 272 and the typhoid death rate is 10/100,000 compared to 45 and 1 in the U. S. A. for these diseases; 40% of the total deaths in Brazil are caused by the infectious agents, less than 18% of the deaths in the U. S. A. are caused by these. In Brazil, 53% of the population is under twenty years of age, in the U. S. A. only 34%. Life expectancy at birth in Brazil is forty years; in the U. S. A. it is sixty-five years. Due to this shortened life-expectancy in Brazil, each producer has more than one dependent, while in the U. S. A. he has only one-half of a dependent. A superimposed comparison of the age-distribution pyramids of the two populations (*Fig.* 2), shows that it is not the cost of the dependent, who later becomes a producer, that is a burden in this high dependent/producer ratio, but that added cost of the dependent, who dies before his twentieth year is the factor of great importance. This is human waste of the most costly type. When the productive potential of two 50,000,000 populations are compared with life-expectancies at birth of forty years and sixty-five years, as in Brazil and the U. S. A., the former has a man-year productive potential of 1,048,000,000 years, the latter 1,506,000,000 years (or 44% greater). Since 75% of the difference is caused by deaths in the age group below twenty years, 348,000,000 man-years are lost to Brazil by premature death. In one generation, Brazil loses 32% of its total productive potential due to premature death. Reduction in infant, juvenile, and adolescent mortality rates will mean a lengthening of life-expectancy and contribute to improvement of both the individual and collective productive potential.

In most under-developed areas, a high percentage of the deaths is caused by infectious agents. These deaths are mostly preventible by modern means. Malnutrition, one of the important causes of shortened life-expectancy, can similarly be controlled with presently available techniques.

There are many more aspects of the economics of illness which could be dwelt upon; the relationship between poverty and disease is direct and forms the hub of a vicious cycle. The greater the poverty, the higher the morbidity and death rate from disease; the higher the death rate, the shorter the productive life span and the greater the loss in pre-productive ages; the greater the losses, the greater the degree of poverty.

Nutritional status, or the adequacy of the diet in a community, is a medico-eco-



AGE DISTRIBUTION PYRAMIDS BRAZIL & U.S.A. SUPERIMPOSED SHOWING AREAS OF DIFFERENCE

FIG. 2. FROM CAMPBELL & MOREHEAD (1953)

nomic problem which relates to the poverty of an area. Work output is in direct proportion to the caloric content of the diet. An adequate diet and hygienic standards, from early childhood, would improve the work output of a population from 50% to 400%.

The lost economic productivity of the physically handicapped, the mentally diseased, and the chronically or incurably ill, is enormous. The National Health Survey of the U. S. A. (1942) showed that on any given day 4.5% of the population is disabled by illness and unable to work. Thus, 7,200,000 are "permanently" ill. Collin[14] (1933) estimated that the annual loss in the U. S. A. due to temporary and permanent disability was between three and four billion dollars. Translating this to today's price and monetary level and present-day population would yield an annual cost of between eight and eleven billion dollars, or between 2% and 3% of the national income.

An estimated 5% of the potential working force of the U. S. A., between three and four million people, are permanently unemployed—the unemployable residue. If this resource could be utilized at the same rate of return as the 62,000,000 presently employed, 18,000,000,000 dollars could be added to our national production.

The cost of the care and treatment of illness must also be considered. Falk[15] estimates that in 1949 when the U. S. A. had a total national income of 217,000,000,000 dollars, about 5% of this, or 10,600,000,000 dollars, was spent on medical and institutional care of the ill.

It is thus well to remember that the standard of living is directly related to usable productivity. *Every illness causes a lowering of the nation's standard of living!*

The economic results of intensive control programs, i.e., practical preventive medicine against selected illnesses have been spectacular—resulting in tremendous monetary savings, repaying many times over the cost of the establishment of the control programs[4,5]. For the communicable diseases, such control pro-

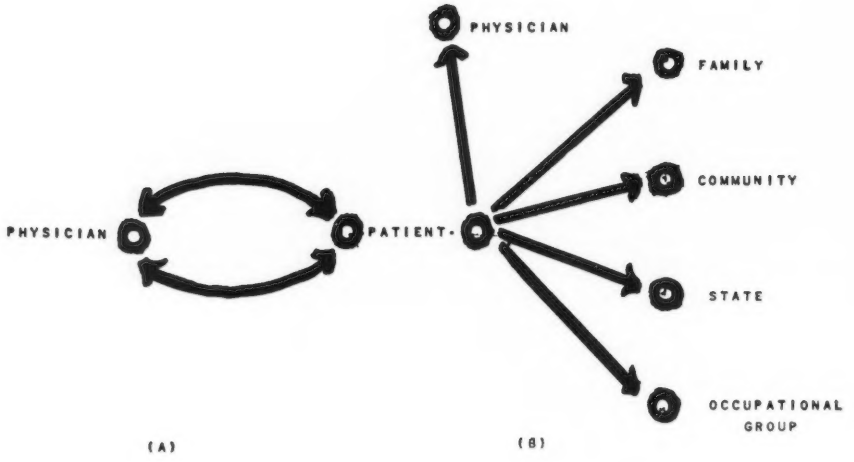


FIGURE 3. THE RELATIONSHIP OF A PATIENT TO HIS SOCIETY AND PHYSICIAN. THIS RELATIONSHIP IS NOT A SIMPLE BINARY AFFAIR (A), BUT RATHER A COMPLEX MULTIPLE ONE (B).

grams can be instituted for as little as 5% to 10% of the savings which result.

3. THE SOCIOLOGY OF ILLNESS (*The role of the patient as a member of society*).

The relation of a patient to the physician is not a simple binary system, but rather a multiphasic system (*Fig.* 3). The patient has obligations to himself, his family, his community, his state, and his occupation. In dealing with the patient as an individual, the physician must keep this in mind. Just as illness in an individual causes an economic dislocation both to the individual and the economic community as a whole; so it also causes a social dislocation in the family which is reflected by disturbances in the more extensive social relationships of the community and state.

An analysis of the social costs and sociology of illness may be examined from two angles: its effects on the social patterns of the patient himself and the effects of illness on society as a whole. Much has been written about both phases. The former demands a knowledge of individual psychology as well as sociology; the latter a knowledge of group psychology.

Kershaw[16], in developing his definition of social medicine—i.e., medicine in relation to social life—points out that man is the province of medicine; hence, all of man's activities must also fall into this sphere. Man is a social animal and all human activities are social and have social aspects and implications. Hence medicine, which is intimately related to human activities, must also be a social study.

We do not have time to dwell on the nature of Society—its anatomy which includes the individual family, the local community, the state, the international community, and the occupational group; its physiology which includes the social contracts, economic relationships, the individual's contribution to Society and Society's rewards to the individual, and the conduct of government; nor its pathology, i.e., the disorders and disharmonies of Society. These are the sinews of classical sociology. All these phases can be interpreted in the light

of the needs of medicine and preventive medicine and public health.

Koos[17], in pointing out that the current shift in emphasis in medical care is from the former focus on the *disease* to a focus on the *patient* who has the disease, as a *person* who has social and psychological relationships that affect his illness, conceives of man's social life as a series of concentric areas with the patient as its center. It is in each of these primary (family) and secondary (community) groups that the impact of illness is felt.

The standard classification of the causes of social problems gives prominence to the biological and psychological agents (acute and chronic illness, physical defectiveness, mental illness and deficiency, etc.) equal to that given the economic and cultural. But except for economic analyses showing lost productive capacity or wealth and the spectacular social disorganization following epidemic outbreaks of communicable diseases or disaster, there have been few detailed analyses made of the pathogenesis and pathological effects of illness on a community. Part of this is due to the incredible complexity of the problem; part due to the failure to apply appropriate techniques. However, the need for such analyses is great. The economic phases, as have been shown, lend themselves to analysis which shows that they are spectacular; however, they are only one facet in the social complex.

On the individual and family level, the changes induced in the social structure are describable in readily understandable terms. These vary widely and depend upon the nature and extent of the illness and the position of the member who is ill. Until adequate quantitative equations of relationships to express this impact are available, the obvious generalizations have little concrete meaning. Varying degrees of psychological and social distress and disorganization may involve various members of the family group. As the social impact of individual illness spreads peripherally into the secondary zones, the force becomes more dilute, but at the same time the total impact is amplified by the sum total of the other illnesses in the community. Here the community organizations which deal with illness must be brought into our equations.

Each medical specialty has its own social problems[19]. There are social problems of surgery, of gynecology and obstetrics, of psychiatry, of industrial medicine, etc.; problems which are distinct in themselves, yet may have the same basic patterns. In addition, the venereal diseases always have been popularly called the "social diseases." In the past, contact with this group of social diseases was about all the physician considered when thinking about social medicine.

There are other social problems of health which rightfully belong to a discussion on the sociology of illness but will not be discussed here. These are, among others, the problem of food and caloric suitability, housing and town planning, work and leisure, sex, genetics and eugenics, and the physically handicapped and rehabilitation. These are only some of the problems wherein the role of medicine and sociology are closely related.

CONCLUSIONS

Health in itself is not the goal of life, but illness is a shackle that frequently prevents man from accomplishing his goal[21]. Illness, however, is as much a social and economic problem as it is a medical problem. From what has been said it can be concluded that *it is within the legitimate province of medicine to seek to restrict these social influences which favor the development of disease;* and further, as Kershaw[16] puts its corollary, *"it lays upon medicine an implied duty to lead social development toward a state of Society which will directly foster positive health."* The physician is in the most favorable position to study the human organism in its entirety, both as a living mechanism and as an essential element of human society[18]."

We have posed the problem which can be summed up in the words of Hall[19] "medicine is no longer an independent profession—a free lance occupation. It has become highly inter-dependent rather than independent, and is carried on

within a framework of elaborate social machinery."

What is organized medicine or the physician doing about this? Current medical education[20] is not developing the requisite skills or training to supply the required specialists. On the contrary, it would seem that the medical organizations spend more time in struggling to maintain a *status quo* and spluttering at the indignities heaped on them than in attempting to meet the challenge. Sigerist[21] commented upon reviewing the place of medicine in a period of transition as follows: "some physicians are fully aware of the trends of the time and have the courage to face the problem openly and to seek its best possible solution, others are afraid of any change. They look back to a past that is gone irrevocably. Trained as highly specialized and efficient scientists, they are unprepared to grapple with problems that are primarily social and economic. They have built for themselves a legendary, sentimental ,and romantic history of their profession to which they cling desperately and which determines their actions."

The leaders of social medicine are, at present, not coming from medicine, but rather from the social and political sciences. Advances in social medicine are being made by the social philosopher, the politician, the trade unions, etc.—groups with little or no medical training. If this trend is permitted to go unchecked, it will take the direction that the sociologist or the politician desires—not necessarily that which is the best from a medical viewpoint.

The practice of medicine is a social activity and to practice it properly, the physician must take a more active interest in social problems. Organized medicine must channel its great energies and give leadership to the development of medicine in relation to social life, as well as influencing social activities in the interest of human well-being.

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SCHOOL NOTES AND NEWS

FACULTY NEWS

Dr. Egon Walter Fischmann, Professor Emeritus and Chairman of the Department of Obstetrics and Gynecology of The Chicago Medical School died Sunday, June 13, 1954 at Grant Hospital in Chicago. The QUARTERLY wishes to join the entire student body, faculty and alumni in expressing their heartfelt sympathy to the family and friends of Dr. Fischmann.

Dr. Fischmann received his medical education at Rush Medical College and in 1906 was granted the degree of Doctor of Medicine. Following internship at Cook County Hospital, he established a large and successful practice in Obstetrics and Gynecology in Chicago. Before his appointment to the staff of The Chicago Medical School, he was Assistant Professor of Gynecology at the Chicago Polyclinic and Associate Professor of Gynecology at the University of Illinois College of Medicine for many years. He served as Professor and Chairman of the Department of Obstetrics and Gynecology at The Chicago Medical School from 1932 until his retirement from active practice in 1952. Since 1952, he had been Professor Emeritus and had continued to act as Chairman of the Department until a successor could be named.

On his seventieth birthday, March 20, 1954, Dr. Fischmann was given a testimonial dinner at the Sherman Hotel. Five hundred people from The Chicago Medical School Faculty, staffs of the two hospitals on which he served, and patients joined to honor him. One of the signal honors of the occasion was the establishment of the Dr. E. W. Fischmann Lectureship in Gynecology at Cook County Hospital.

Dr. Fischmann was a Fellow of the American College of Surgeons, Fellow of the American Medical Association, and a member of the Central Association of Obstetricians and Gynecologists, Chicago Medical Society, Illinois State Medical Society, Chicago Institute of Medicine, Chicago Gynecological Society and the German Medical Society of Chicago. He was consulting Obstetrician and Gynecologist at Grant Hospital, Attending Gynecologist at Cook County Hospital and Professor of Gynecology at the Cook County Graduate School of Medicine and was certified by the American Board of Obstetrics and Gynecology.

During his many years on the Faculty of The Chicago Medical School, Dr. Fischmann devoted himself to his teaching duties and became one of the most respected and beloved faculty members. He will always be remembered as a source of inspiration and guidance to the many physicians and students who enjoyed the privilege of studying with him.

NEW CURRICULUM ANNOUNCED

President John J. Sheinin has announced that the curriculum committee of The Chicago Medical School has revised the curriculum of the junior and senior years. The purposes of these revisions is to make full use of the new clinical and hospital facilities which have become available to the school and to provide the student with more clinical experience during his formal medical education. These revisions were made possible by the recent affiliation of The Chicago Medical School with Michael Reese Hospital and the West Side Veterans' Administration Hospital. These new clinical facilities will be added to those already in use at Mount Sinai Hospital and Cook County Hospital. The school plans to maintain and strengthen its association with all four institutions.

Under the new program the junior year will consist of three quarters and the senior year of four quarters. Each quarter is twelve weeks in length and there is a one week recess between each quarter. During the junior year one quarter will be devoted to a combination of didactic lectures and clinics. The following courses will be given each week:

Lectures:	
Dermatology	Two hours
Public Health	Three hours
Therapeutics	One hour
Radiology	One hour
Oncology	One hour
Clinics:	
Dermatology	One hour
Orthopedic Surgery	Two hours
Psychiatry	Two hours
Urology	Two hours
Pediatrics	Two hours
New-Born	One hour
Contagious Diseases	One hour
Gynecology	Two hours
Neurology	Two hours
Ophthalmology	Two hours
Otorhinolaryngology	Two hours

The remaining two quarters of the junior year will be devoted to two six-week clerkships in Medicine and two six-week clerkships in Surgery. Each clerkship will be spent at a different hospital, so that each student will spend six weeks at Mount Sinai Hospital, Michael Reese Hospital, Cook County Hospital and the West Side Veterans' Administration Hospital. Each clerkship group will consist of six students with one full-time instructor in charge. These small clerkship groups will make possible more personal contact between student and instructor.

The senior year will consist of four quarters. Two quarters will be spent in the Out-Patient Clinics at Mount Sinai Hospital. The third quarter will be spent in a combined Medical and Surgical Clerkship on the internship level at Mount Sinai Hospital. This senior clerkship is designed to give the student educational opportunities and responsibilities equal to those obtained during internship. The fourth quarter will be divided into six weeks of Pediatric Clerkship and six weeks of Obstetrical Clerkship. The Pediatric Clerkship will be spent at Cook County Children's Hospital, while the Obstetrical Clerkship will consist of two weeks each at Mount Sinai Hospital, Michael Reese Hospital, and The Chicago Maternity Center.

These improvements in the teaching program are in keeping with the aim of The Chicago Medical School to constantly improve medical education and produce more competent doctors.

FACULTY APPOINTMENTS

President John J. Sheinin has announced the appointment of Dr. Aaron E. Kanter as Professor and Chairman of the Department of Obstetrics and Gynecology. It is with great pride that the QUARTERLY joins the Faculty and student body in extending a warm welcome to Dr. Kanter.

Born in 1894 in Harrisburg, Pennsylvania, Dr. Kanter received his education in Chicago, Illinois. He attended the University of Chicago and received the degree of Bachelor of Science in 1914. In 1915 he received the degree of Master of Science from the same institution. He pursued his medical education at Rush Medical College and in 1917 he was granted the degree of Doctor of Medicine. He was licensed to practice medicine in Illinois in 1917. He served his internship at Cook County and Presbyterian Hospitals.

In 1918 his medical education was interrupted by the First World War. Dr.

Dr. Aaron Kanter

Kanter served in the Medical Corps of the United States Navy for 14 months as a Lieutenant Senior-Grade. Following his discharge from the Armed Forces, Dr. Kanter resumed his post-graduate medical education, specializing in Obstetrics and Gynecology. He studied at Trinity College in Dublin, the University of Glasgow, the Universities of Paris and Bordeaux and at the University of Vienna. Dr. Kanter then returned to Chicago to the private practice of Obstetrics and Gynecology.

In 1921 he was appointed an Assistant in Obstetrics and Gynecology at Rush Medical College. He was promoted to Instructor in 1924, Assistant Professor in 1925, Associate Professor in 1928 and in 1937 he became a full Professor of Obstetrics and Gynecology. He remained in this position until 1944 when he was appointed Rush Professor of Obstetrics and Gynecology at the University of Illinois College of Medicine. Recently Dr. Kanter has been serving as Professor and Chairman of the Department of Obstetrics and Gynecology at the Cook County Graduate School of Medicine.

Despite a very successful private practice and his extensive activities in the field of medical education, Dr. Kanter has found time to publish over forty scientific papers dealing with problems in the field of Obstetrics and Gynecology. He is a Fellow of the American College of Surgeons, Fellow of the American Medical Association, member of the Society of Sigma Xi, Associate Attending Obstetrician and Gynecologist at Presbyterian Hospital and Attending Gynecologist at Cook County and Mount Sinai Hospitals. He has been certified by the American Board of Obstetrics and Gynecology and is a member of the Central Association of Obstetricians and Gynecologists, Chicago Institute of Medicine, Chicago Medical Society, Illinois State Medical Society and a member and past president of the Chicago Gynecological Society.

In his new position, Dr. Kanter will serve as Professor and Chairman of the Department of Obstetrics and Gynecology as a member of the faculty on a half-time basis. We trust that his association with The Chicago Medical School will be long and mutually beneficial.

President John J. Sheinin has announced the following full-time appointments to the faculty of The Chicago Medical School:

Department of Medicine

Dr. Emanuel E. Mandel as Associate Professor in Medicine.

Born in 1910 in Vienna, Austria, Dr. Mandel received his medical education at the University of Vienna where he was granted the degree of Doctor of Medicine in 1934. He served an internship at the University Hospital in Vienna.

After arriving in the United States, he was licensed to practice Medicine in New York in 1939 and was certified by the American Board of Internal Medicine in 1944. He has been on the staff of the Metropolitan Hospital in New York City and Grady Memorial Hospital in Atlanta, Georgia. He has taught at the New York Medical College as an Assistant Instructor in Medicine and at Emory University School of Medicine as an Assistant Professor of Medicine and Clinical Pathology.

Dr. Mandel served in the United States Public Health Service as a Senior Surgeon (Lieutenant-Colonel) from 1945 to 1954. He did post-graduate work at Northwestern University and was granted the degree of Master of Science in

1950. He is a member of numerous scientific organizations, including the American College of Physicians and Sigma Xi, and has published over thirty scientific papers.

Dr. Esther R. Pizer as Associate in Medicine.

Dr. Pizer was born in Chicago in 1917 and received her education at the University of Illinois. She received the degree of Doctor of Medicine in 1941, served her internship at Cook County Hospital and her residency in Internal Medicine at Cook County Hospital and the Lahey Clinic in Boston. She has been a Clinical Assistant in the Department of Medicine at the University of Illinois School of Medicine and Northwestern University School of Medicine. She has been on the staffs of Columbus Hospital, Michael Reese Hospital and Cook County Hospital and Director of the Allergy Clinic at Women's and Children's Hospital in Chicago.

Dr. Pizer is a member of many scientific and honorary organizations including Alpha Omega Alpha, Chicago Society of Allergy and Chicago Tuberculosis Society.

Dr. Earl N. Silber as Associate in Medicine.

Born in 1921 in Milwaukee, Wisconsin, Dr. Silber was educated at the University of Wisconsin where he was granted the degree of Doctor of Medicine in 1945. He served his internship and residency at Michael Reese Hospital in Chicago and was certified by the American Board of Internal Medicine in 1953. Since July, 1952 he has been Assistant Director of Medical Education at Michael Reese Hospital.

Dr. Silber, whose main interest is in the field of Cardiology, is a member of numerous scientific organizations including the American College of Physicians, American Heart Association and the American Federation of Clinical Research. He has seen service as a Captain in the United States Army Medical Corps and has published over twenty scientific papers.

Dr. Arthur A. Billings as Instructor in Medicine.

Dr. Billings, who was born in Chicago in 1925, received his education at the University of Illinois School of Medicine where he was granted the degree of Doctor of Medicine in 1950. He served his internship and residency at Michael Reese Hospital in Chicago. He is a member of Alpha Omega Alpha and other scientific organizations.

Dr. Morton Smith as Instructor in Medicine.

Dr. Smith, who was born in 1922 in Baltimore, Maryland, received his education at the University of Maryland where he was granted the degree of Doctor of Medicine in 1950. He served his internship at Michael Reese Hospital and is a member of Alpha Omega Alpha.

Dr. Louis Richmond as Clinical Instructor in Medicine.

Dr. Richmond was born in Brooklyn, New York in 1922. He attended The Chicago Medical School and was granted the degree of Doctor of Medicine in 1946. He served his internship at Methodist Hospital, Gary, Indiana and took his postgraduate work at the Veterans' Administration Hospital in Columbia, South Carolina and Mount Sinai Hospital in Chicago. He is on the staff of Edgewater and Mount Sinai Hospitals. He recently was discharged from the United States Army Medical Corps after serving twenty-four months as a Captain.

Department of Pathology

Dr. Henry Rappaport as Associate Professor of Pathology.

Dr. Rappaport was born in Lvov, Poland in 1913. He received his medical education at the University of Vienna where he was granted the degree of Doctor of Medicine in 1937. He did postgraduate work at the University of Montpellier in France from 1938 to 1940.

After arriving in the United States, Dr. Rappaport served an internship at Michael Reese Hospital in Chicago and a residency in Pathology at Mount Sinai Hospital in Chicago. He has been Attending Pathologist and Chief of the Laboratory Service at the Veterans' Administration Hospital in Washington, D. C. and has served as Pathologist at the

Armed Forces Institute of Pathology. He has also been an Assistant Professor of Pathology at George Washington School of Medicine.

Dr. Rappaport served as a Major in the United States Marine Corps during the last war. He is a member of many scientific organizations, including the American College of Physicians, College of American Pathologists and American Association for the Advancement of Science. He has published many scientific papers.

Dr. J. D. Wheeler as Instructor in Pathology.

Born in Missouri in 1924, Dr. Wheeler received his medical education at Northwestern University where he was granted the degree of Doctor of Medicine in 1950. He served his internship at Kansas City General Hospital. He took his postgraduate work at Washington University Medical School and Harvard University Medical School, and taught at both institutions. He served as an Ensign in the United States Navy for thirty-three months.

Department of Physiology and Pharmacology

Dr. Jean A. Sice as Assistant Professor of Pharmacology.

Dr. Sice was born in Paris, France and received his education at the University of Marseille. He was granted the degrees of Bachelor of Arts in 1936, Bachelor of Science in 1937, Doctor of Philosophy in 1943 and Master of Science in 1945. He taught at the University of Marseille as Instructor in Pharmacology from 1942 to 1948 and at the University of Chicago School of Medicine as Instructor in Surgery from 1948 until 1951.

Dr. Sice served as a Lieutenant in the French Army Medical Corps during the last war. He is a member of the American and Swiss Chemical Societies and in 1945 was the recipient of the Perron Award of the French Academy of Medicine.

Department of Microbiology

Dr. Julius Goldberg as Assistant Professor of Microbiology.

Born in 1927 in Birmingham, Alabama, Dr. Goldberg received his education at the University of Kentucky where he was granted the degree of Doctor of Philosophy in 1951. He has served as a Research Associate at the University of Tennessee, Research Fellow at the University of Louisville College of Medicine and Assistant Professor of Bacteriology and Director of the Virus Diagnostic Laboratory at the Medical College of South Carolina.

Dr. Goldberg is a member of the Society of American Bacteriologists, American Venereal Disease Association and Sigma Xi. He has also published many scientific papers. During the last war, he served in the Medical Corps of the United States Army.

Department of Pediatrics

Dr. Lester Wishingrad as Clinical Assistant in Pediatrics.

Dr. Wishingrad was born in 1927 in Brooklyn, New York. He was graduated, with the degree of Doctor of Medicine, from The Chicago Medical School in 1951. He served his internship at Queens General Hospital in New York and his residency at Children's Hospital, Akron, Ohio and the University of Illinois Department of Pediatrics. He received the C. V. Mosby Award in 1952. During the last war, Dr. Wishingrad served in the United States Navy.

Dr. Sheinin has also announced the following additional appointments to the faculty of The Chicago Medical School:

Dr. Jules Gelperin as Clinical Assistant Professor in Neurology and Psychiatry.

Dr. Bernard Chomet as Associate Professor in Clinical Pathology.

Dr. Morris Arnkoff as Clinical Associate in Urology.

Dr. Murray Friedman as Research Associate in Pathology.

Dr. Robert A. Atkins as Clinical Instructor in Surgery.

Dr. Charles Myran as Clinical Instructor in Psychiatry.

Dr. Robert F. Jeans as Clinical Instructor in Psychiatry.

Dr. William Schumer as Clinical Instructor in Surgery.

Dr. Louis A. Goldberg as Clinical Instructor in Dermatology.

Dr. Maurice J. Sherman, Jr. as Clinical Assistant in Medicine.

Dr. Sidney M. Goldman as Clinical Assistant in Urology.

Dr. Gilbert Iser as Clinical Assistant in Ophthalmology.

Dr. Gerschen L. Schaefer as Clinical Assistant in Medicine.

The QUARTERLY wishes to express its congratulations to these men and women on their appointments to the Faculty of The Chicago Medical School and to bid them welcome.

ALUMNI NEWS

Class of 1939:

Congratulations to Dr. and Mrs. Herbert Tashman on the birth of their son, Bob Frederic, on March 15, 1954.

Class of 1940:

Congratulations to Dr. Louis Berlin on his appointment as Assistant Professor of Neurology at Cornell University Medical College.

Class of 1942:

The QUARTERLY extends its best wishes to Dr. Julius Brant upon the opening of his office for the practice of Medicine at 18139 South Torrence Avenue, Lansing, Illinois.

Congratulations to Dr. Hyman Love upon his certification by the American Board of Radiology. Dr. Love recently completed a three year residency in Radiology at St. Luke's Hospital, Chicago, Illinois.

Class of 1945:

The QUARTERLY was very happy to receive a letter recently from Dr. Kenneth M. Calhoun. Dr. Calhoun is engaged in the practice of Obstetrics and Gynecology at 513 East Grove Street, Bloomington, Illinois.

Class of 1946:

Dr. Emanuel Chusid is a Resident in Pediatrics at New York Medical College, Flower and Fifth Avenue Hospitals. He recently completed a similar residency at The Bronx Hospital, New York, New York.

Best wishes to Dr. Benedict Egon Liewen upon the occasion of his marriage to the former Miss Jane Caryl Reske on June 26, 1954.

Dr. Marvin F. Loring has recently returned to the United States after studying at the Royal Cancer Hospital of London. He studied under a British-American Exchange Fellowship in Cancer Research which is sponsored by the American Cancer Society.

Best wishes to Dr. Sidney Malitz upon resumption of his practice of Psychiatry at 40 East 83rd Street, New York City. Dr. Malitz recently returned from military service.

Congratulations to Dr. and Mrs. Eugene J. Rogers on the birth of their son, Jay Alan Lighter Rogers, on April 12, 1954.

Congratulations to Dr. Normabelle H. Shively on her appointment to the Bexar County Health Board. Dr. Shively is in practice at 2326 Cincinnati Avenue, San Antonio, Texas.

Class of 1947:

Dr. Albert B. Chatzinoff has been awarded a traineeship at the National Institute of Neurological Diseases and Blindness, Mount Sinai Hospital, New York City.

Best wishes to Dr. and Mrs. Sidney P. Helfer on the birth of their son, Jeffrey Brian, on March 26, 1954.

Dr. Seymour Levine has been awarded a traineeship in Pathology at Montefiore Hospital, New York City.

Class of 1948:

Congratulations to Dr. and Mrs. Stanley Reichman on the birth of their daughter, Erica, on March 3, 1954.

Class of 1949:

Best wishes to Dr. and Mrs. Milton R. Bronstein on the birth of their daughter, Arna Beth, on March 8, 1954.

Congratulations to Dr. and Mrs. James W. Fletes on the birth of their daughter, Eva Jane, on August 18, 1954.

The QUARTERLY wishes to congratulate Dr. Bernard Halperin upon the opening of his office for the practice of Internal Medicine at 361 Westward Drive, Miami Springs, Florida.

Congratulations to Dr. and Mrs. Sidney Kase on the birth of their son, Charles, on August 8, 1954.

Best wishes to Dr. and Mrs. Bernard Kleppel on the birth of their daughter, Lisa Joan, on August 17, 1954.

Congratulations to Dr. Seymour Werthamer upon his appointment as Pathologist and Chief of Clinical Laboratories at Mount Sinai Hospital, Hartford, Connecticut.

Class of 1950:

Congratulations to Dr. William W. Anderson upon his appointment as a Senior Resident in Neurology at University Hospital, Ann Arbor, Michigan.

Dr. Lawrence D. Elegant has completed a residency in Pediatrics at the Sarah Morris Hospital for Children of the Michael Reese Hospital and has become associated with Dr. Alfred B. Stein for the practice of Pediatrics in Chicago. Dr. Elegant recently received the Borden Award from the Chicago Pediatric Society for a paper, *Methemoglobin Studies in Premature Infants, Full Term Mature Infants, Children and Adults.*

Dr. Herbert L. Fishbein, at present, is associated with the Lakeside Medical Center, Detroit, Michigan. Dr. Fishbein is engaged in the practice of Radiology.

The QUARTERLY extends its best wishes to Dr. Abraham S. Ludwig on the opening of his office at Old Country Road, Plainview, Long Island.

Congratulations to Dr. Louis Lunsky on the occasion of his marriage to the former Miss Eugenie Bowman on June 20, 1954. Dr. Lunsky has recently opened an office for the practice of Psychiatry at 6310 West Olympic Boulevard, Los Angeles, California.

We wish to congratulate Dr. Philip Oransky upon the opening of his office for the practice of Internal Medicine at 6045 Eighth Street, Tamiami Trail, Miami, Florida.

Congratulations to Dr. Gerschen L. Schaefer upon completion of his residency in Internal Medicine at Mount Sinai Hospital, Chicago, Illinois. Dr. Schaefer has been appointed Assistant to the Director of the Chest Department at Mount Sinai Hospital, Assistant to the Medical Director of Winfield Hospital and is on the staff of both hospitals. He has also been appointed Clinical Assistant in the Department of Medicine at The Chicago Medical School.

Congratulations to Dr. and Mrs. Maurice J. Sherman on the birth of their daughter, Francine, on March 7, 1954. Dr. Sherman has recently completed a residency in Internal Medicine at the Veterans' Administration Hospital, Hines, Illinois and has been appointed Clinical Assistant in Medicine at The Chicago Medical School.

Class of 1951:

The QUARTERLY extends its best wishes to Dr. Walter A. Charles upon the opening of his office for the practice of Pediatrics at 614 E. Genesee Street, Syracuse, New York.

Congratulations to Dr. and Mrs. Lester Cohn on the birth of their daughter, Miriam Esther, on January 17, 1954.

Dr. Charles Fadem, after completing his internship and one year of residency in Internal Medicine at Kings County Hospital, Brooklyn, New York, is now a First Lieutenant in the United States Air Force. He is stationed at the 3700th United States Air Force Hospital, Lackland Air Force Base, San Antonio, Texas.

Congratulations to Dr. and Mrs. Marvin S. Freedland on the birth of their son, Gary Allan, on April 7, 1954.

Congratulations to Dr. Sanford F. Gaylord upon the announcement of his association with Drs. Rosenblum, Neidus, Firestone and Zlotnick for the practice of Internal Medicine at the Medical Center, 318 Fifth Avenue, Youngstown, Ohio.

Congratulations to Dr. and Mrs. Stanley Leithold on the birth of their daughter, Naomi Gail, on June 4, 1954.

We wish to congratulate Dr. and Mrs. George Magid on the birth of their son, Paul David, on May 21, 1954. Dr. Magid is a Resident in Internal Medicine at the Virginia Mason Hospital and Clinic, Seattle, Washington.

Dr. Louis W. Silver has recently been discharged from the United States Air Force after serving for 18 months in Korea where he received a commendation from the Surgeon-General of the 5th Air Force. He is now a Resident in Obstetrics and Gynecology at Beth-El Hospital, Brooklyn, New York.

Class of 1952:

Dr. Sanford Cohen is now a second

year Resident in Psychiatry at Duke University Medical Center.

The QUARTERLY wishes to extend its best wishes to Dr. Arnold Grier on the opening of his office for the practice of General Medicine at 350 Lincoln Road, Miami Beach, Florida.

The QUARTERLY extends its best wishes to Dr. Marvin Markowitz upon the opening of his office for the practice of Medicine at 3298 Cherry Wood Drive, Wantagh, Long Island.

Class of 1953:

Dr. Edward Berkwits has completed one year of interneship at Cook County Hospital, Chicago, Illinois and plans to remain for an additional six months of training.

Best wishes to Dr. Philip Bonn on his marriage to the former Miss June Ray of McCaub, Mississippi on June 11, 1954.

Congratulations to Dr. and Mrs. Sander J. Breiner on the birth of their daughter, Linda Marie, on May 4, 1954.

Dr. Marvin R. De Haan has completed one year of internship at Cook County Hospital, Chicago, Illinois and plans to remain for an additional six months of training before entering General Practice.

Dr. Harold M. Fischer has entered the Post-Graduate School of Basic Sciences for the first part of his training in Surgery.

Dr. Harold R. Galef has been appointed to the staff at the United States Public Health Service Hospital, Fort Worth, Texas.

Congratulations to Dr. Milton Glickstein on his marriage to the former Miss Beverly Edelman.

Best wishes to Dr. Morton J. Gollub on his marriage to the former Miss Joan Lopinson.

Best wishes to Dr. and Mrs. John S. Horning on the birth of their daughter, Ann Elizabeth, on January 27, 1954. Dr. Horning is a Resident in Surgery at Milwaukee County Hospital, Milwaukee, Wisconsin.

Dr. Robert Jensen has completed one year of internship at Cook County Hospital, Chicago, Illinois and plans to remain for an additional six months of training before entering General Practice.

Dr. Robert J. Langs has been appointed to the staff of the United States Public Health Service Hospital, Lexington, Kentucky.

Congratulations to Dr. Gene W. Mason upon his engagement to Miss Lucille Winkler of Chicago, Illinois. Dr. Mason, at present, is a First Lieutenant in the United States Air Force.

Congratulations to Dr. Herschel H. Solomon on his marriage to the former Miss Joan Newman of Central City, Iowa on November 1, 1953.

Dr. Richard Telingator has been appointed to the staff of the Out-Patient Clinic of the United States Public Health Service, Washington, D. C.

Class of 1954:

The QUARTERLY wishes to congratulate the members of the Class of 1954 upon their graduation from The Chicago Medical School on June 26, 1954. The commencement, at which the sixty-nine graduating seniors were awarded the degree of Doctor of Medicine, was held at the Murphy Auditorium of the American College of Surgeons. The commencement address was presented by Reverend Adalbert R. Kretzmann, Pastor of the Evangelical Lutheran Church of Saint Luke, Chicago, Illinois.

Dr. Sidney O. Levinson, former Director of the Michael Reese Research Foundation, was awarded posthumously an honorary degree of Doctor of Science. Dr. Levinson, who died on June 20, 1954, had a long and distinguished career as director of the research programs of the Michael Reese Foundation.

The Dr. M. L. Parker Awards for meritorious research by members of the faculty of The Chicago Medical School were presented to Drs. Aldo A. Luisada and Emanuel Marcus. The John J. Sheinin Award, for the member of the graduating class who shows outstanding scholarship, excellence of character, and professional competence, was presented to Dr. Stanley Bauer. Citations, for services on the staff of The Chicago Medical School Quarterly, were presented to Drs. Theodore Feldman, Melvin Samuels, Hubert Segal and Lawrence Shuman.

We wish to congratulate Dr. Theodore Feldman of Rockaway Beach, New York,

on his marriage to the former Miss Judy Ellen Rivkin of Far Rockaway, New York on September 5, 1954.

Congratulations to Dr. and Mrs. Hubert Segal on the birth of their son, Fredric Alan, on May 26, 1954.

Best wishes to Dr. Samuel P. Shattan of Brooklyn, New York on his marriage to the former Miss Sharan Goldstein of Chicago, Illinois.

STUDENT NEWS

Class of 1955:

The Class of 1955 is pleased to announce the following results of its recent election of officers for the Senior Year:

President—Herbert Bengelsdorf
Vice-President—Sheldon Gross
Secretary—Jerome Goldstein
Treasurer—Milton Greenberg
Student Council Representatives—Edward Altchek, Howard Weinstein.

The QUARTERLY extends congratulations and best wishes to:

Edward Altchek on his marriage to the former Miss Marilyn Pearl of New York City on June 24, 1954.

Arnold Brody upon his marriage to the former Miss Lita Gray of Chicago on June 27, 1954.

Melvin and Estelle Greenblatt on the birth of their daughter, Beth Myra, on September 9, 1954.

Herbert Sohn on the occasion of his marriage to the former Miss Norma Fisch of New York City. Mr. Sohn has recently been appointed Student Editor of The Journal of the Student American Medical Association for the academic year 1954-55.

Bud and Vera Stahlecker on the birth of their daughter, Karen Lee, on June 14, 1954.

Ernest M. and Renee Weitz on the birth of their daughter, Susan Ann, on May 6, 1954.

Stuart and Frances Eichenfield on the birth of their son, Andrew Howard, on September 14, 1954.

Stanley Becker of St. Louis, Missouri on his engagement to Miss Sandra Orth of Evanston, Illinois.

Herbert Blough of Philadelphia, Pennsylvania on his engagement to Miss Racelle Miller of Chicago, Illinois.

Class of 1956:

The QUARTERLY extends its congratulations and best wishes to:

Herbert and Carol Aronson on the birth of their daughter, Jaclyn, on June 21, 1954.

Jesse S. Gochman upon his marriage to the former Miss Frances Flower of Peekskill, New York on June 27, 1954.

Leonard Parr on his marriage to the former Miss Joyce Selma Hokin of Peoria, Illinois on July 4, 1954.

Class of 1957:

The QUARTERLY extends congratulations and best wishes to:

Ted Bayless upon the occasion of his marriage to the former Miss Janet Nides of Mount Vernon, New York on June 22, 1954.

Murray Belsky upon his engagement to Miss Arlene Yonowitz of Newark, New Jersey.

Malvin Cole on his marriage to the former Miss Susan Kugel on June 20, 1954.

Jordan B. Greenfield of Brooklyn, New York on the occasion of his marriage to the former Miss Sheila Brown of Winthrop, Massachusetts on June 20, 1954.

Irwin L. Hirsch upon his marriage to the former Miss Enid Aaron of Brooklyn, New York on June 27, 1954.

Jordan Katz upon his marriage to the former Miss Ruby Reiter of Brooklyn, New York on June 27, 1954.

Robert Lilien upon his engagement to Miss Sondra Geller of Hillside, New Jersey.

Gene Schwartzman upon his marriage to the former Miss Gwen Bunin of Brooklyn, New York on June 20, 1954.

Arnold Serbin upon his marriage to the former Miss Barbara Ainbinder of Brooklyn, New York on June 27, 1954.

Jerry Siegel upon his marriage to the former Miss Ruth Isaacs of North Bergen, New Jersey on June 22, 1954.

RESIDENCY APPOINTMENTS

We wish to congratulate the following members of the class of 1953 on their recently announced residency appointments:

Lawrence Adler—Surgery, Henry Ford Hospital, Detroit, Michigan.

Norman Bacher—Psychiatry, University Hospital, Baltimore, Maryland.

Harry M. Bauer—Pathology, Cedars of Lebanon Hospital, Los Angeles, Calif.

Donald J. Behr — Internal Medicine, Kings County Hospital, Brooklyn, New York.

Frederick Berkowitz—Otorhinolaryngology, Veterans' Administration Hospital, Long Beach, California.

Philip Bonn—Orthopedic Surgery, Kennedy Veterans' Administration Hospital, Memphis, Tennessee.

Sander J. Breiner—Psychiatry, Pontiac State Hospital, Pontiac, Michigan.

Solomon Chazan — Pediatrics, Kings County Hospital, Brooklyn, New York.

Ralph Cobrinik—Pediatrics, Flower and Fifth Avenue Hospitals, New York, New York.

Kenneth D. Cohen—Psychiatry, Philadelphia Psychiatric Hospital, Philadelphia, Pennsylvania.

Milton Glickstein—Surgery, Mount Sinai Hospital, New York, New York.

Jerome Gold—Internal Medicine, Kings County Hospital, Brooklyn, New York.

Morton J. Gollub—Internal Medicine, Albert Einstein Memorial Center, Philadelphia, Pennsylvania.

Jesse D. Greenberg—Internal Medicine, Maimonides Hospital, Brooklyn, New York.

Alex M. Greenberger—Internal Medicine, Veterans' Administration Hospital, Brooklyn, New York.

Bernard Gussoff—Internal Medicine, Veterans' Administration Research Hospital, Chicago, Illinois.

Jack Handel—Radiology, Jewish Hospital of Brooklyn, Brooklyn, New York.

Jerome L. Handler, Internal Medicine, Veterans' Administration Research Hospital, Chicago, Illinois.

Arthur J. Henning—Pediatrics, Los Angeles County Hospital, Los Angeles, California.

John Horning—Surgery, Milwaukee General Hospital, Milwaukee, Wisconsin.

Stanley Jaffe, Surgery, Mount Sinai Hospital, Cleveland, Ohio.

Samuel Kessler—Internal Medicine, Cook County Hospital, Chicago, Illinois.

Donald A. Klotz — Internal Medicine, Queens General Hospital, New York.

Marvin Kranis—Internal Medicine, Veterans' Administration Hospital, Brooklyn, New York.

Seymour F. Kuvin, Pediatrics, Saint Michael's Hospital, Newark, New Jersey.

Sheldon Lichtblau — General Surgery, Bronx Hospital, Bronx, New York.

Irwin Miller—Surgery, Maimonides Hospital, Brooklyn, New York.

Arthur Pinchuck — Internal Medicine, Jewish Hospital of Brooklyn, Brooklyn, New York.

Martin Rubinstein — Pathology, Mount Zion Hospital, San Francisco, Calif.

Marvin C. Rulin—Radiology, Mount Sinai Hospital, Cleveland, Ohio.

Melvin M. Schiff—Pathology, Montefiore Hospital, Pittsburgh, Pennsylvania.

Larry Schneck—Pediatrics, Jewish Hospital of Brooklyn, Brooklyn, New York.

Myron R. Schoenfeld—Internal Medicine, Kingsbridge Veterans' Administration Hospital, Bronx, New York.

Marilyn Schwab — Psychiatry, Kings County Hospital, Brooklyn, New York.

Eugene P. Shatkin—Internal Medicine, Highland-Alameda County Hospital, Oakland, California.

Herschel Solomon — Internal Medicine, Veterans' Administration Hospital, Brooklyn, New York.

Lawrence Strick — Pediatrics, Kaiser Foundation Hospital, Oakland, Calif.

Philip Sumner—Internal Medicine, Beth Israel Hospital, New York, New York.

James Terrano—Surgery, Saint Rita's Hospital, Lima, Ohio.

Himeo Tsumori — Pediatrics, Highland-Alameda County Hospital, Oakland, California.

Gerald Weiner—General Surgery, Veterans' Administration Hospital, Aspinwall, Pennsylvania.

Herman Ziffer — Internal Medicine, Roosevelt Hospital, New York, N. Y.

THE CHICAGO MEDICAL SCHOOL INTERNESHIPS
CLASS OF JUNE, 1954

Abrams, Martin W.—
Cook County Hospital
Chicago, Illinois

Adicoff, Arnold—
Mount Sinai Hospital
Cleveland, Ohio

Bauer, Stanley—
The Mount Sinai Hospital
New York, New York

Berger, Allan M.—
Kings County Hospital
Brooklyn, New York

Bernson, Lionel A.—
Kings County Hospital
Brooklyn, New York

Blatt, Meyer—
Harbor General Hospital
Torrance, California

Blumberg, Bernard—
Albert Einstein Medical Center, Southern Division
Philadelphia, Pennsylvania

Boodin, Bernard B.—
Newark Beth Israel Hospital
Newark, New Jersey

Braunstein, Leonard—
Philadelphia General Hospital
Philadelphia, Pennsylvania

Cerfolio, Robert D.—
Kings County Hospital
Brooklyn, New York

Cohen, Frederick B.—
Jewish Hospital of Brooklyn
Brooklyn, New York

Etzel, Edward—
The Presbyterian Hospital of Chicago, Chicago, Illinois

Fader, Alfred—
Mount Sinai Hospital
Cleveland, Ohio

Feldman, Theodore—
Hospital for Joint Diseases
New York, New York

Feuerman, Lawrence—
Maimonides Hospital
Brooklyn, New York

Fisch, Herbert J.—
Kings County Hospital
Brooklyn, New York

Fishkin, Seymour—
Cook County Hospital
Chicago, Illinois

Foster, Lois G.—
The Presbyterian Hospital of Chicago, Chicago, Illinois

Graivier, Leonard—
Cook County Hospital
Chicago, Illinois

Igdaloff, Irving—
Cook County Hospital
Chicago, Illinois

Jacobs, Walter H.—
Kings County Hospital
Brooklyn, New York

Jacobson, York G.—
Los Angeles County Hospital
Los Angeles, California

Jacoby, Arthur W.—
Newark Beth Israel Hospital
Newark, New Jersey

Kalt, Wallace B.—
Meadowbrook Hospital
Hempstead, New York

Kaplan, Sanford A.—
Kings County Hospital
Brooklyn, New York

Keller, Marvin—
Beth Israel Hospital
New York, New York

Keuer, James R.—
Milwaukee County Hospital
Milwaukee, Wisconsin

King, Edward J.—
Hackensack Hospital
Hackensack, New Jersey

Kleinman, Edwin—
Los Angeles County Hospital
Los Angeles, California

Lattimer, Agnes D.—
Cook County Hospital
Chicago, Illinois

Leibsohn, Eugene—
Los Angeles County Hospital
Los Angeles, California

Levinson, Marvin S.—
Cook County Hospital
Chicago, Illinois

Lieb, Herbert E.—
Newark Beth Israel Hospital
Newark, New Jersey

Lovell, Norman C.—
Veterans' Administration Hospital, Long Beach, California

Malerstein, Abraham J.—
Cook County Hospital
Chicago, Illinois

Matles, Arthur L.—
Jewish Hospital of Brooklyn
Brooklyn, New York

McMeel, James E., Jr.—
Milwaukee County Hospital
Milwaukee, Wisconsin

Meyer, Saul N.—
Kings County Hospital
Brooklyn, New York

Michel, Jules H.—
Cook County Hospital
Chicago, Illinois

Mosovich, Ervin—
Newark Beth Israel Hospital
Newark, New Jersey

Oliner, Herman L.—
The Mount Sinai Hospital
New York, New York

Orr, Israel—
Michael Reese Hospital
Chicago, Illinois

Paul, George J.—
Meadowbrook Hospital
Hempstead, New York

Pesin, Arthur D.—
Hackensack Hospital
Hackensack, New Jersey

Post, Melvin—
Beth El Hospital
Brooklyn, New York

Robin, Leon—
Michael Reese Hospital
Chicago, Illinois

Rosenberg, Jerry—
University of Minnesota Hospital, Minneapolis, Minnesota

Rosenblatt, Howard M.—
Cook County Hospital
Chicago, Illinois

Ruben, Richard F.—
Mount Sinai Hospital
Cleveland, Ohio

Samuels, Melvin H.—
Los Angeles County Hospital
Los Angeles, California

Schein, Sheldon L.—
Kings County Hospital
Brooklyn, New York

Segal, Hubert B.—
Jewish Hospital of Brooklyn
Brooklyn, New York

Shapiro, Norman M.—
Mount Zion Hospital
San Francisco, California

Sharoff, Jerrold L.—
Beth Israel Hospital
New York, New York

Shattan, Samuel P.—
Beth El Hospital
Brooklyn, New York

Sherman, Eugene—
Michael Reese Hospital
Chicago, Illinois

Shuman, Lawrence H.—
Albert Einstein Medical Center, Southern Division
Philadelphia, Pennsylvania

Snyder, Herbert L.—
Manchester Memorial Hospital, Manchester, Connecticut

Sobel, Harold J.—
Kings County Hospital
Brooklyn, New York

Sporn, Max—
Kings County Hospital
Brooklyn, New York

Stone, Sam H.—
Los Angeles County Hospital
Los Angeles, California

Trachtenberg, Eugene—
Kings County Hospital
Brooklyn, New York

Trow, Jerome A.—
Kings County Hospital
Brooklyn, New York

Warman, Marvin—
Kings County Hospital
Brooklyn, New York

Weiler, Martin E.—
Kings County Hospital
Brooklyn, New York

Weinert, Sanford D.—
District of Columbia General
Hospital, Washington, D.C.

West, Michael—
Cook County Hospital
Chicago, Illinois

Zibelman, Warren B.—
Cook County Hospital
Chicago, Illinois

Zimmerman, Saul L.—
Beth Israel Hospital
New York, New York

Socio-Economic Costs of Illness —

(Continued from page 30)

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Dorolle, P.: (1953) "World Health and Economic Development," Chronicles World Health Org. 7(10):274-279.

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Amyotrophic Lateral Sclerosis —

(Continued from page 21)

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BOOK REVIEWS

MODERN CLINICAL PSYCHIATRY by Arthur P. Noyes, M.D. Cloth. Fourth Edition. 609 pages. Philadelphia: W. B. Saunders Company, 1953. $7.00.

This fourth edition of this popular general textbook of psychiatry contains many revised and many completely new sections. Psychological influences and motivations in the production of personality disorders are emphasized in this edition. The principles of basic psychiatry are presented more fully and genetic and dynamic concepts are expanded. The author presents many of the important currently accepted psychoanalytical concepts, although he is is not a psychoanalyst. Mental disorders are classified according to the standard nomenclature of the American Psychiatric Association. There is an excellent bibliography at the end of each chapter. This book is highly recommended to medical students, and invaluable to psychiatrists and persons in allied fields such as social work and psychology.

* * * *

MAYO CLINIC DIET MANUAL by The Committee on Dietetics of the Mayo Clinic. Cardboard loose-leaf. Second Edition. 247 pages. Philadelphia: W. B. Saunders Company, 1954. $5.50.

This second edition is completely revised and is based on the latest information on food, vitamins and current dietary practices at the Mayo Clinic.

Recommendations are based on the 1953 revision of the Recommended Dietary Allowances of the National Research Council. Vitamin information follows the latest revision of the United States Pharmacopeia. Changes from the first edition have been made in the following dietary programs: "dumping syndrome," postcolostomy, ileostomy and bowel resection, sprue, hyperlipoidemia, cardiorenal diseases, underweight, and diabetes. The standard tube feeding has been changed and two new tables have been aded, *viz.*, the trial diet for food elimination and a table showing the caloric values of beverages and snack foods. This manual should be in every hospital kitchen and library. The general practitioner, surgeon and internist will find this book to be indispensable.

* * * *

CLINICAL DISORDERS OF THE HEART BEAT by Samuel Bellet, M.D. Cloth. First Edition. 373 pages. Philadelphia: Lea and Febiger, 1953. $8.50.

The author has limited this text to a subject which has long been an enigma to the student of medicine, both at and beyond the medical school level. In well-organized fashion, Dr. Bellet has attempted to provide a guide to the diagnosis and treatment of the cardiac arrhythmias. The subject matter is divided into four sections, the first of which deals with the general characteristics of arrhythmias. The second section is a discussion of the individual arrhythmias, with particular stress given to clinical features. The third section deals with the arrhythmias in association with certain clinical states, such as Rheumatic Fever. Syncope, Pregnancy, Congenital Anomalies, Thyroid Disease, and many others. The fourth section concerns itself with digitalis, quinidine, and Pronestyl, the three primary drugs in the treatment of the arrhythmias. Both the Table of Contents and Index are well-prepared, enabling one to easily locate material in the text. Numerous boxed summaries are provided throughout the text, and provide a quick reference in a "point-by-point" fashion for subjects of special importance. The text is recommended for medical students and general practitioners, as well as for internists and cardiologists.

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RHEUMATIC DISEASES by Eugene F. Traut, M.D., F.A.C.P. Cloth. First Edition. 942 pages with 192 illustrations. Philadelphia: W. B. Saunders Company, 1952. $20.00.

This well-written and thorough text has certainly fullfilled the intentions of the author, namely "to be understandable to the medical student, of practical use to the internist and the physician in general practice, and valuable as a reference and source book to the rheumatologist." Dr. Traut's style is very readable and the print is extra large, both factors being a treat for the suffused eyes of the medical student. References are numerous and up-to-date and are placed conveniently at the bottom of each page. The book is replete with photographs, diagrams and x-rays all of which are well-reproduced. The index is adequate. This book is indeed a valuable reference and source book not only to the rheumatologist, but to anyone desiring accurate, informative and comprehensive information on the diagnosis and treatment of the rheumatic diseases. The book is highly recommended.

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DISEASES OF THE DIGESTIVE SYSTEM by Sidney A. Portis, M.D., F.A.C.P. Cloth. 1119 pages with 269 engravings and 5 color plates. Philadelphia: Lea and Febiger, 1953. $20.00.

Dr. Sidney Portis has recruited the advice and assistance of a very excellent and representative group of clinicians from all parts of the country in the preparation of this third edition of *Diseases of the Digestive System.* Much stress has been placed on the relation between the psyche and the soma and the effects of these relationships on the gastrointestinal system and its disorders. This approach is very aptly provided by the cooperation of psychiatrists and gastroenterologists in individual chapters. Eight new chapters have been added, among which

are Hyperinsulism and Fatigue, and The Effect of Sulfonamides and Antibiotics on the Intestinal Flora. Readability has been enhanced by increased page size and new type. Up to date references are provided at the end of each chapter. The Index and Table of Contents are very complete and permit ready accessibility to the text material. This book is recommended to the internist and student, and provides an especially valuable source of information for those interested in psychosomatic and gastro-intestinal problems.

* * * *

FUNDAMENTALS OF OTOLARYNGOLOGY — a Textbook of Ear, Nose, and Throat Diseases by Lawrence R. Boies, M.D. Second Edition. Cloth. 487 pages with 197 figures. Philadelphia and London: W. B. Saunders Company, 1954. $7.00.

Dr. L. R. Boies' *Textbook of Otolaryngology* is a remarkably good book for both the medical student and the general practitioner. Unlike many of the larger tomes of otolaryngology, it does not purport to be a "complete reference" book, but rather attempts to present a wealth of practical information concerning diseases of the ear, nose and throat — their diagnosis and treatment. Of particular value to the student and the busy general practitioner are the chapters dealing with the normal anatomy, physiology, and examination of the ear, nose, and throat. The book is well-printed in a pleasant, large type. A remarkable number of illustrations well-accompany the text, which, in itself, has a very smooth-flowing style. This book is not recommended for those who wish a reference book in otolaryngology.

* * * *

CLINICAL MANAGEMENT OF BEHAVIOR DISORDERS IN CHILDREN by Harry Bakwin, M.D. and Ruth Morris Bakwin, M.D. Cloth. 495 pages. Philadelphia: W. B. Saunders Company, 1953.

The twelve sections of this book deal with the growth and development of the child, the normal variations in behavior and then the behavior problems and psychosomatic diseases with their etiologies and management. The first two sections deal adequately with the physical and psychological growth and development of the child. An emphasis is placed on normal variation and is especially valuable. The section on the care of the physically ill and handicapped child, often neglected in the training of the physician, has many interesting suggestions compactly presented. For example, the discussion of deafness includes incidence, etiology, testing, mental functioning, personality, schooling, occupational opportunities, care and training.

The section on psychosomatic disease suffers somewhat from the lack of an analytically oriented discussion of the child's problems. However, this book was not written primarily for the psychiatrist, but for the general practitioner, the pediatrician, psychologist, and social worker and it adequately fulfills this purpose. Of special interest to the physician is the treatment of cerebral damage in relation to brain disorders and the differential diagnosis of cerebral from primary behavior disorders. Other sections such as those on intelligence and intelligence testing are of more interest to the psychologist.

Totally, this is an excellent, concise reference text for the busy physician who is faced with these problems in his practice. The book is attractively printed and well-bound. The references are complete and the index generous.

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A MANUAL OF TROPICAL MEDICINE by Thomas T. Mackie, M.D., George W. Hunter, III, Ph.D. and C. Brooke Worth, M.D. Cloth. Second Edition. 907 pages with 304 illustrations, 7 in color. Philadelphia: W. B. Saunders Company, 1954.

This is the second edition of this popular book, the first edition of which was published during World War II, as one of a group of volumes prepared under the auspices of the National Research Council for the use of the Armed Forces. Necessarily, at that time, the *Manual* consisted of a concise presentation of the essential aspects of the epidemiology, diagnosis, treatment, control and prophylaxis of the more important tropical diseases. Much new information has accumulated since the first edition and the authors have been stimulated to prepare a new edition in which several sections have been completely, or largely, rewritten by distinguished collaborators in their respective fields. Increased field experience of the authors has led to the inclusion of new chapters covering the virus encephalitides, trachoma, rickettsialpox, trench fever, leptospiral diseases, leprosy, toxoplasmosis, gnathostomiasis, trichostrongyliasis, the nutritional diseases, effects of heat, epidemic hemorrhagic fever and medically important molluscs.

The book is well-bound, well-indexed and contains numerous well-reproduced charts and photographs. It is highly recommended both to the medical student and to the general practitioner who can expect to see more and more of the so-called "tropical" diseases as travel to tropical climates becomes more attainable and hence more common.

* * * *

THE BIOCHEMISTRY OF CLINICAL MEDICINE by William S. Hoffman, M.D. Cloth. 681 pages. Chicago: The Year Book Publishers, Inc., 1954. $12.00.

The aim of this book is to acquaint the student and the practitioner alike with the qualitative and quantitative alterations of the biochemically determinable body constituents, which occur in disease, and to show how to utilize this information in diagnosis, prognosis, and treatment of disease. As such, it is an extremely

valuable book which demonstrates the dynamics of the disease process from the biochemical point of view.

The book was planned for the student and general practitioner with no more than the usual training in chemistry and physiology. The author's wide experience as an undergraduate and postgraduate teacher places him in an especially qualified position to have written this book. Although there is an attempt to avoid highly technical explanations or chemical formulae, the text loses nothing in thoroughness and should prove more than adequate to those concerned with review for board examinations.

This book is highly recommended for all students and practitioners because of its success in integrating the basic sciences with clinical medicine, without which the rational practice of medicine is impossible.

* * * *

GENERAL CYTOLOGY by E. D. P. DeRobertis, W. W. Nowinski, and Francisco A. Saez. Cloth. Second Edition. 456 pages with 162 illustrations. Philadelphia and London: W. B. Saunders Company, 1954.

Even more than the First, the Second Edition of *General Cytology* should be read by all medical students who have some spare time, and by all practitioners of medicine. It is fascinatingly written so that it is good entertainment.

De Robertis, Nowinski, and Saez cover a very wide range of knowledge of many aspects of cell life from chemical organization to morphology and cellular physiology. It is a distinct contribution of the present book to have, for the first time . . . given a comprehensive account of the tremendous advances in this field during the last forty-two years.

Other very recent work that is well-covered is in the field of ultrathin section electronmicroscopy.

Totally, the book is quite indispensable for the research worker . . . in many fields . . . as well as for the medical man's library.

Dr. Hans Elias

* * * *

CURRENT THERAPY, 1954. Edited by Howard F. Conn, M.D., with a Board of 12 Editorial Consultants. Cloth. 850 pages. Philadelphia: W. B. Saunders Company, 1954. $11.00.

This is the sixth of an annual series of volumes devoted to the most recent approved methods of treatment. The material presented is not extracted from the literature but represents the methods used in practice today by the physicians who comprise the editorial board. A goodly portion of the material is simply a repetition of discussions in the previous volume. However, more than one hundred of the methods in this 1954 volume are new.

Some representative subjects discussed in the current volume are: Cortisone in bronchiectasis, intermittent positive pressure breathing in silicosis, Rauwolfia Serpentina in treatment of hypertension, newer anticoagulants in myocardial infarction, and Aureomycin for acute viral pericarditis. The text is brisk, concise, and readable. The index is excellent. Every practicing physician should have this most useful boook on treatment on his desk for ready reference.

* * * *

THE THYROID by Thomas Hodge McGavack, B.A., M-D., F.A.C.P., *et. al.* Cloth. 646 pages with 67 illustrations. St. Louis: The C. V. Mosby Company, 1951. $14.00.

Thomas Hodge McGavack has attempted to present in this book material concerning the most recent work in the physiology, patho-physiology, and histo-pathology of the thyroid gland. There also are brief, but adequate sections dealing with historical and surgical considerations of the thyroid gland.

The author states that the purpose of the book is to summarize the recent advances for the use of "undergraduate student, investigator, and internist alike." It probably achieves this purpose quite well but appears, to the reviewer, to be of somewhat too great detail for use by the student except as a source of reference material.

There is a voluminous bibliography well-suited for the research worker. Illustrations are extremely few in number, the author referring the reader to original source material for illustrations.

* * * *

DISEASES OF WOMEN by Robert J. Crossen, M.D., F.A.C.S. Cloth. Tenth Edition. 935 pages with 990 illustrations. St. Louis: C. V. Mosby Company, 1953. $18.50.

This long-awaited Tenth Edition of Crossen's *Diseases of Women* has successfully attempted to continue to present "the basic facts and salient developments of biologic and physiologic investigations," and to bring to the practitioner "a comprehensive systematic judicial consideration of the diagnostic and therapeutic aids made possible by these great advances." Well-situated and well-reproduced illustrations, as well as a very readable type of print, add to the value of the text. In keeping with the many other advances in the field, more emphasis has been placed on the psychosomatic aspects of gynecologic problems. All of the developments in diagnostic techniques, which have been recognized in the twelve years that have elapsed since the previous edition, have been incorporated. These include: the vaginal smear; culdoscopy; culpocentesis; and many others. Treatment has been brought up to date and a new section on radiation therapy has been added. As in previous editions, an adequate Table of Contents and a thorough Index allows one to locate any subject with ease. This book is recommended to the student and general practitioner as well as to the gynecologist.

ABSTRACTS SECTION

BASERGA, RENATO *(Assoc. in Oncology)* and SHUBIK, PHILLIPPE *(Asst. Prof. and Conductor of Oncology, Dept. of Surgery).* The action of Cortisone on transplanted and induced tumors in mice. Cancer Research, *14* (1): 12-16, 1954.

Investigations in mice with a transplantable adenocarcinoma and with methylcholanthrene induced tumors of the skin and of the subcutaneous tissues have been carried out. Repeated injections of cortisone have been found to give rise to an increase in the rate of metastatic diffusion of all these tumors, and to an inhibition in the induction of the skin tumors.

* * * *

BOLONICK, S. J. *(Assoc. in Pediatrics),* Lobar Emphysema, Proc. of Inst. of Med. of Chicago, 25:50 (February 15), 1954.

This case report is presented because of its relative rareness and because of the difficulty in making a differential diagnosis.

This male infant was delivered by low forceps and cried spontaneously. There were no abnormalities.

At 6 weeks of age the infant suddenly developed dyspnea and cyanosis. X-ray revealed a shifting of the mediastinum to the right with considerable emphysema of the entire left lung. Bronchoscopy revealed the trachea deviated to the right and the left main bronchus was markedly obstructed by compression. A diagnosis of lobar emphysema was made, and the infant submitted to surgery.

Upon opening the chest the emphysematous upper lobe bulged out of the wound. The lobe was removed and the chest closed. A few days later, X-ray of the chest showed the mediastinum shifted back to its normal position. The child made an uneventful recovery.

The differential diagnosis rests between congenital heart disease, atelectasis, agenesis of the lung, congenital cyst, foreign bodies and diaphragmatic hernia. However without any evidence of acute infection, the diagnosis of lobar emphysema can easily be made in an infant with a history of sudden onset of dyspnea and cyanosis early in life.

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CONGDEN, E. D. (*Emeritus Prof. of Anat.*) and FISH, H. S. (*Asst-Prof. of Micro-Anat.*), The Chief Insertion of the Bicipital Aponeurosis is on the Ulna, Anatomical Record, *110*:395-407, 1954.

There are a number of human flat tendons that, to the casual observer, seem to lose their identity by mingling with muscle ("deep") fascia. Since tendons are of a more compact texture than fascia, it seems doubtful that they could give over their pull to the looser structure of fascia. The bicipital aponeurosis of the biceps humeri muscle was taken as an example of these tendons and its collagenous bundles dissected under a hand lens. One very fine sheet which the aponeurosis gives off was studied in microscopic sections. Many of the bundles of the aponeurosis were traced directly to the dorsal ulnar border. Others combined with bundles of antebrachial fascia to reach a similar attachment. Delicate bands bent down to reach the tendons of origin of the pronato-flexor mass at an angle of about 90°.

The aponeurosis, although wrapped around the pronato-flexor mass, can have no pulley action nor is there a supinating action. Pull of the aponeurosis on the ulna, as it has one-fourth the cross section of the radial tendon, somewhat balances it in the volar flexion of the forearm.

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DAVIDSOHN, ISRAEL *(Prof. and Chairman, Dept. of Pathology)* and STERN, KURT *(Assoc-Prof. of Pathology),* Heterohemoantibodies in Inbred Strains of Mice. II. Immune Agglutinins and Hemolysins for Sheep and Chicken Red Cells, J. Immunol., *72*:216-223 (March), 1954.

The antibody response to two heterologous hemoantigens, sheep and chicken erythrocytes, was studied in over 1600 healthy, tumor-free mice belonging to eleven different inbred strains. Titers of immune agglutinins and hemolysins were found to be distributed in fairly constant patterns characteristic for each individual strain, whereas significant inter-strain differences became apparent with regard to mean titers of the immune hemoantibodies. Antibodies for sheep and chicken erythrocytes were independent of each other, as shown by absorption experiments and by the failure of injection of one antigen to raise titers for the other. Immune response to administration of sheep erythrocytes was not correlated to presence of natural agglutinin for sheep red cells, while such a correlation was found to exist between natural agglutinins and immune antibodies for chicken erythrocytes. Differences in antibody response was observed in two sublines of strain DBA. These findings suggested that genetic factors may be, at least in part, responsible for the degree of immune response of mice to hemoantigens. Passive immunization with homologous serum failed to support the assumption that differences in metabolic rate may be responsible for high or low antibody levels in mice of different strains. Ranks were assigned to each individual strain, based on statistical tests of significance which were applied to the mean titers. When these ranks were tabulated, five of the six high-tumor or high-leukemia strains were found to show lower levels of immune hemoantibodies than the five low-tumor, low-leukemia strains tested.

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FASOLI, A., MAGID, E. B., GLASSMAN, M. D. and FOA, P. P. *(Dept. of Physiology),* Serum Lipoproteins in Experimental Diabetes. I. Lipoprotein Pattern of Normal and Depancreatized Dogs, Proc. Soc. Exp. Biol. & Med., *85*:609, 1954.

The serum lipoproteins of normal and depancreatized dogs have been studied by means of paper electrophoresis. Dog serum contains three main lipoprotein fractions: albumin-alpha-globulin, beta globulin, and beta$_2$-gamma globulin. The bulk of the serum lipids is carried by the albumin-alpha-globulin fraction. Although the serum of depancreatized dogs under insulin control contains a greater amount of cholesterol than the serum of normal dogs, the lipoprotein fractions are not significantly different from normal. The withdrawal of insulin is followed by an immediate increase of all lipoprotein fractions. As decompensation sets in, the beta globulin fraction increases out of proportion to the other fractions. The results suggest that diabetic decompensation is associated with lipoprotein abnormalities similar to those suspected of having a pathogenic relationship to atherosclerosis in man.

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HURWITZ, PAUL *(Asst. Prof. of Ophthalmology)*, Mandibulofacial Dysostosis, AMA Archives of Ophth., *51*:1 (January), 1954.

A new case of Mandibulofacial Dysostosis (Franceschetti's disease, Treacher-Colins' syndrome, craniofacial hemiatrophy) is presented, together with a summary of the history and features of the syndrome. Only 38 cases have been previously reported.

The chief features of the syndrome are 1) antimongoloid palpebral fissures with lid colobomata; 2) malar bone and mandibular hypoplasia; 3) ear malformations; 4) macrostomia, high palate, irregular dispositions of the teeth, and malocclusion; 5) blind fistulae between the angles of the mouth and ears; 6) atypical hair growth from hairline to cheek; 7) facial clefts, and 8) skeletal deformities, such as missing thumbs. A fish-like or bird-like face is characteristic.

Classification of the syndrome includes five forms: 1) complete, 2) incomplete, 3)abortive (lid anomalies only), 4) unilateral, and 5) atypical.

The syndrome is hereditary and evolves from delayed ossification of the mesodermally derived facial bones of the first visceral arch.

Features not previously reported, described in this case, are 1) widening of the sella turcica, 2) accentuated digital impressions of the skull, 3) dolichocephaly, and 4) defective inferior orbital margins.

Mandibulofacial Dysostosis must be differentiated from 1) cleidocranial dysostosis, 2) craniofacial dysostosis (Crouzon), and 3) acrocephaly with syndactyly.

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STERN, KURT *(Assoc. Prof. of Path.)* and DAVIDSOHN, ISRAEL *(Prof. and Chairman, Dept. of Pathology)*. Heterohemoantibodies in inbred strains of mice. I. Natural agglutinins for sheep and chicken red cells, J. Immunol., 72:209-215 (March), 1954.

In extension of earlier work, natural agglutinins for sheep red cells were detetermined in over 1800 mice of thirteen inbred strains, and agglutinins for chicken red cells in over 1500 mice belonging to twelve inbred strains. Considerable inter-strain differences relating to occurence and mean titers of both hemagglutinins were noted. Natural hemolysin for sheep red cells was never found, natural hemolysin for chicken red cells only rarely and in low titers. Natural agglutinins for human red cells were rare in all strains, and low-titered when present.

Cross-absorption experiments demonstrated complete independence of sheep and chicken hemoantibodies from each other. By means of suitable statistical methods, the signifcance of inter-strain differences between mean titers of sheep and chicken hemagglutinins was established, and on that basis ranks were assigned to each individual strain. Ranks based on titers of natural sheep agglutinins showed no correlation to spontaneous incidence of tumors or leukemia in the strains tested; on the other hand, comparison of mean titers of chicken agglutinins showed that six low-tumor strains exhibited high mean titers whereas low mean titers were observed in five out of six high-tumor or high-leukemia strains. Discussion of the possible causes and significance of the differences in natural hemoantibodies in mice took into consideration the operation of genetic factors, differences in antigenic composition of mouse tissues, and innate immune response. The latter factor appeared of particular interest in connection with studies on immune hemoantibodies in mice of inbred strains, which form the subject of a separate report.

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TAUB, S. J. *(Prof. of Medicine)* and ROSENBERG, H.W. Passive Transfer Tests as an Aid in Persistent Bronchial Asthma, Postgrad. Med., *15:1;* 54-56 (January), 1954.

Recently there has been a marked trend on the part of certain allergists to magnify the importance of psychogenic factors in the etiology of bronchial asthma. It has been our experience, over a number of years, in a large series of patients, that neurogenic and psychogenic factors are by themselves only contributory or accessory causes and do not alone provoke attacks of bronchial asthma.

We have always believed that it is of prime importance to study the patient thoroughly with every method at the disposal of the allergist, starting with a careful, detailed, exhaustive history, laboratory studies, x-ray and fluoroscopy of the chest, complete intra-dermal tests, and finally the method of passive transfer.

The passive transfer method of testing (Prausnitz-Kustner) is probably not used as often as it should be by allergists. A patient with severe uncontrollable asthma, age eighteen, is cited who gave negative reactions to important allergens because she was receiving antihistaminic drugs, adrenalin and ephedrine, which interfered with the direct positive skin tests. Etiologic factors were found and the results of therapy were most gratifying in this patient and several others in this series.

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THE CHICAGO MEDICAL SCHOOL
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1955

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Dr. Rachmiel Levine, Chairman of the Department of Medicine, Director of Metabolic and Endocrine Research, Michael Reese Hospital.

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